Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

The Total Synthesis of the Oxopolyene Macrolide RK-397

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General Information. All reactions were conducted in oven-dried glassware under a dry nitrogen atmosphere. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketal under nitrogen. Dichloromethane (CH_2Cl_2), toluene, triethylamine, diisopropylamine, and *N,N*-diisopropylethylamine were distilled from CaH_2 under nitrogen. Dimethyl sulfoxide was distilled from CaH_2 under reduced pressure. Acetone and methanol were dried over $CaSO_4$ then distilled under nitrogen from CaH_2. Trimethylsilyl trifluoromethanesulfonate was distilled under nitrogen prior to use. Titanium(IV) isopropoxide and (+)-diisopropyl L-tartrate were distilled under reduced pressure prior to use. Methyl acetoacetate was washed with 1:1 brine / saturated sodium bicarbonate, dried over magnesium sulfate, and fractionally distilled under ambient atmosphere. Benzene, chlorobenzene, (1S)-(+)-3-carene (90%), *p*-anisaldehyde dimethyl acetal, oxalyl chloride, chloromethyl methyl ether, dibutylboron triflate (1.0M in CH_2Cl_2), diethyl methoxyborane, diisobutylaluminum hydride (1.0M in hexanes), trimethylphosphite, benzylidene-bis(tricyclohexylphosphine)dichlororuthenium (Grubbs' 1st generation catalyst), triethyl phosphonoacetate, and 2,4,6-trichlorobenzoyl chloride were purchased from the Aldrich Chemical Company and used as received. A solution of *tert*-butyl hydroperoxide in isooctane was prepared and titrated using Sharpless' method[1] and dried over 4Å molecular sieves prior to use. Molecular sieves were dried overnight in a vacuum oven (1-2 mm Hg, 130 °C) and stored in an oven at 145 °C. Desispheres were obtained from Scientific Adsorbents Incorporated and stored in an oven at 145 °C. Thin layer chromatography was performed using EM Science Silica Gel 60 F_{254} glass plates. Flash chromatography was performed using 60 Å silica gel (32-63 μm). ^{1}H NMR spectra were obtained at 500 or 400 MHz and ^{13}C NMR spectra at 125 or 100 MHz in $CDCl_3$, C_6D_6, or CD_3OD as indicated. Chemical shifts are reported in ppm referenced to

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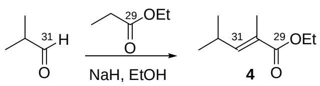
[1] Y. Gao, R. M. Hanson, J. M. Klunder, S. Y. Ko, H. Masamune, K. B. Sharpless, *J. Am. Chem. Soc.* **1987**, *109,* 5765-5780.

$CHCl_3$ (7.24 ppm for ^{1}H) and $CDCl_3$ (77.0 ppm for ^{13}C), C_6D_5H (7.15 ppm for ^{1}H) and C_6D_6 (128.4 ppm for ^{13}C) or CD_2HOD (3.31 ppm for ^{1}H) and CD_3OD (49.0 ppm for ^{13}C). IR spectra were recorded as thin films on NaCl plates. Optical rotations were determined using a Jasco P-1030 polarimeter and concentrations are reported as g / 100 mL. Exact mass was determined as M+H or M+Na as indicated. Gas chromatography was carried out using an Alltech SE-54 column (achiral stationary phase) or a Supelco β-dex 120 column (chiral stationary phase) using hydrogen as the carrier gas. Combustion analyses were performed by NuMega Resonance Labs, Inc. of San Diego, CA.

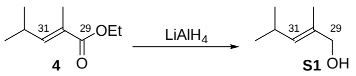
2,4-Dimethyl-pent-2-enoic acid ethyl ester (4):



To a cooled (0 °C) suspension of sodium hydride (52.66 g, 60 wt% in mineral oil, 1.3 mol, 1.3 equiv) in ethyl propionate (475 mL, 4.14 mol, 4.0 equiv) was added ethanol (4.0 mL, 69 mmol, 0.066 equiv) by syringe, resulting in the evolution of hydrogen gas. Isobutyraldehyde (74.81 g, 1.037 mol, 1.0 equiv) was then added portionwise by cannula over 30 min. After stirring 30 min at 0 °C, the reaction was diluted with hexanes (100 mL), quenched by slow addition of saturated sodium bicarbonate, and further diluted with water (100 mL). The layers were separated and the aqueous phase was extracted with hexanes (4x). The combined organic extracts were dried ($MgSO_4$) and concentrated at atmospheric pressure to an oil. Distillation of the product at reduced pressure (*ca.* 20 mm Hg) provided the known[2] ester **4** as a clear, yellow oil (> 50:1 *E*:*Z*, 104.45 g, 668.59 mmol, 64%) with the following spectral characteristics:

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.54 (dq, J = 10, 1 Hz, 1H), 4.16 (q, J = 7 Hz, 2H), 2.56-2.66 (m, 1H), 1.81 (d, J = 1 Hz, 3H), 1.27 (t, J = 7 Hz, 3H), 1.00 (d, J = 7 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6, 148.8, 125.6, 60.4, 27.9, 22.0, 14.3, 12.3.

2,4-Dimethyl-pent-2-en-1-ol:



To a cooled (0 °C) suspension of lithium aluminum hydride (18.9 g, 498 mmol, 4.4 equiv "H^-") in ether (1 L, undistilled, freshly opened canister) was added a solution of ester **4** (70.13 g, 448.9 mmol, 1.0 equiv) in ether (200 mL) by cannula over 25 min. The resulting mixture was allowed to warm to room temperature over several hours as the ice melted and was stirred for a total of 17.5 h. The reaction was then quenched by slow addition of 150 mL 3M sodium hydroxide, resulting in the formation of a white precipitate. The mixture was stirred for 10 min then filtered through a glass frit, washing repeatedly with ether. Distillation at atmospheric pressure (bp 153.5-156 °C) afforded 40.6 g of the known alcohol **S1**[2] which displayed the following spectral characteristics:

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.19-5.23 (m, 1H), 3.96 (dd, J = 6, 1 Hz, 2H), 2.46-2.56 (m, 1H), 1.65 (d, J = 1 Hz, 3H), 1.23 (t, J = 6 Hz, 1H), 0.93 (d, J = 7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 133.9, 132.3, 69.0, 26.8, 22.9, 13.6. A portion (55.20%) of this mixture was used in the next reaction without additional purification.

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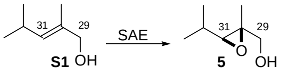
[2] V. J. Lee, A. R. Branfman, T. R. Herrin, K. L. Rinehart, *J. Am. Chem. Soc* **1978**, *100*, 4225-4236.

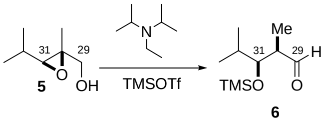
(3-Isopropyl-2-methyl-oxiranyl)-methanol (5):



To a cooled (-20 °C) mixture of 3 Å molecular sieves (powdered, 6.33 g), (+)-diisopropyl L-tartrate (5.0 mL, 24 mmol, 0.12 equiv), and titanium (IV) isopropoxide (5.8 mL, 20 mmol, 0.10 equiv) in CH_2Cl_2 (560 mL) was added *tert*-butyl hydroperoxide (70 mL, 5.6 M in isooctane, 390 mmol, 2.0 equiv) by a pressure-equalizing addition funnel over 10 min. The addition funnel was rinsed with CH_2Cl_2 (10 mL), and the resulting mixture was stirred for 30 min at –20 °C. A solution of **S1** (22.41 g, 196.3 mmol, 1.0 equiv) in CH_2Cl_2 (53 mL) was pre-dried over 1.5 g 4Å molecular sieves for 110 min then added dropwise by the addition funnel, and the funnel was rinsed with CH_2Cl_2 (10 mL). The resulting mixture was stirred for 1 h at –20 °C then warmed to 0 °C and poured into a cooled (0 °C) suspension of Iron (II) sulfate (76.59 g) and tartaric acid (22.08 g) in water (350 mL). The resulting mixture was stirred for 15 min, and the aqueous phase was saturated with solid sodium chloride and extracted with CH_2Cl_2 (9x). Emulsions were formed in some of the extractions, and were dispersed by filtration through celite.[1] The organic phases were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. Distillation under reduced pressure (b.p. 87-97 °C, 21-30 mm Hg) afforded the known epoxy alcohol[3] **5** (21.22 g). Analysis by gas chromatography with a chiral stationary phase showed 95.8 % ee (Supelco β-Dex 120, isothermal at 75 °C, 1.7 mL/min flow rate, t_{major} = 31.9 min, t_{minor} = 30.3 min). The crude product was used directly in the next reaction, and displayed the following spectral characteristics:

^1H NMR ($CDCl_3$, 500 MHz): δ 3.66 (dd, J = 12, 4 Hz, 1H), 3.56 (dd, J = 12, 9 Hz, 1H), 2.70 (d, J = 9 Hz, 1H), 1.63 (dd, J = 9, 4 Hz, 1H), 1.48-1.58 (m, 1H), 1.28 (s, 3H), 1.08 (d, J = 7 Hz, 3 H), 0.93 (d, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 65.9, 65.5, 61.4, 27.6, 20.1, 18.5, 14.1.

2,4-Dimethyl-3-trimethylsilanyloxy-pentanal (6):



To a cooled (-78 °C) solution of alcohol **5** (21 g, 160 mmol, 1.0 equiv) and *N,N*-diisopropylethylamine (39 mL, 220 mmol, 1.4 equiv) in CH_2Cl_2 (820 mL) was added trimethylsilyl trifluoromethanesulfonate (38 mL, 210 mmol, 1.3 equiv) dropwise by cannula over 15 min. The resulting solution was stirred for 1 h at –78 °C then quenched by addition of pH 7 buffer (250 mL) and allowed to warm to room temperature. The mixture was diluted with pentane and the phases separated. The organic phases were washed with saturated copper (II) sulfate (2x) and brine (2x), then dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure to give the known aldehyde[4] **6** (32.37 g) as a clear yellow oil. The crude product was analyzed by gas chromatography (Alltech SE-54, isothermal at 75 °C, 1.1 mL/min flow rate, t_{major} =

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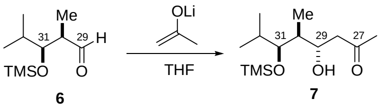
[3] R. Göttlich, U. Schopfer, M. Stahl, R. W. Hoffmann, *Liebigs Ann. Chem.* **1997**, 1757-1764.

[4] D. A. Evans, B. D. Allison, M. G. Yang, C. E. Masse, *J. Am. Chem. Soc.* **2001**, *123*, 10840-10852.

11.4 min, t_{minor} = 12.0 min) which revealed a diastereomeric ratio of 24:1. The crude product was used directly in the next step and displayed the following spectral characteristics:

^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.69 (d, J = 1 Hz, 1H), 3.80 (dd, J = 7, 4 Hz, 1H), 2.48 (ddq, J = 7, 4, 1 Hz, 1H), 1.72 (octet, J = 7 Hz, 1H), 1.07 (d, J = 7, 3H), 0.89 (d, J = 7 Hz, 3H), 0.86 (d, J = 7 Hz, 3H), 0.06 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.3, 77.0, 50.3, 31.8, 19.6, 18.7, 8.0, 0.6.

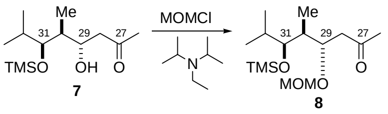
4-Hydroxy-5,7-dimethyl-6-(trimethyl-silanyloxy)-octan-2-one (7):



To a cooled (-78 °C) solution of diisopropylamine (29 mL, 210 mmol, 1.3 equiv) in THF (576 mL) was added *n*-butyllithium (129 mL, 1.5 M in hexanes, 190 mmol, 1.2 equiv) by cannula over 10 min. The resulting cloudy mixture was stirred for 10 min at -78 °C, then acetone (14 mL, 190 mmol, 1.2 equiv) was added dropwise by syringe. The resulting mixture was stirred for 30 min at -78 °C, then cooled to –100 °C. A solution of aldehyde **6** (32.37 g, 160.0 mmol, 1.0 equiv) in THF (56 mL) was then added by cannula down the side of the flask over 8 min. The reaction mixture was stirred for 1 h at -100 °C, then quenched by the addition of saturated ammonium chloride (250 mL) and allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3x). The combined organic phases were washed with brine, dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. ^{1}H NMR analysis of the crude product revealed a diastereomeric ratio of 10:1. Purification by flash chromatography (7.75:1 hexanes/ethyl acetate) provided diastereomerically pure hydroxyketone **7** (23.60 g), as well as mixed fractions which were resubjected to flash chromatography (dichloromethane then 100:1 dichloromethane/ethyl acetate then 9:1 dichloromethane/ethyl acetate) to provide a total yield of diastereomerically pure **7** of 25.37 g (98.80 mmol, 40% from **4**) as a clear, colorless oil.

R_f: 0.50 (3:1 hexanes/ethyl acetate); the minor isomer has R_f: 0.43 (3:1 hexanes/ethyl acetate). $[\alpha]_D$ = -33.7 (*c* 1.54, CH_2Cl_2). IR: 3494, 2953, 2912, 2871, 1709, 1248 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (ddt, J = 9, 3, 3 Hz, 1H), 3.67 (dd, J = 8, 2 Hz, 1H), 3.35 (d, J = 3 Hz, 1H), 2.72 (dd, J = 17, 2 Hz, 1H), 2.45 (dd, J = 17, 10 Hz, 1H), 2.18 (s, 3H), 1.59-1.73 (m, 2H), 0.92 (d, J = 7 Hz, 3H), 0.81 (d, J = 7 Hz, 3H), 0.74 (d, J = 7 Hz, 3H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 77.5, 69.0, 48.1, 40.7, 31.4, 30.8, 20.2, 19.6, 10.0, 0.8. Anal. calcd. for $C_{13}H_{28}O_3Si$: C 59.95, H 10.84. Found: C 59.60, H 10.44.

4-Methoxymethoxy-5,7-dimethyl-6-(trimethyl-silanyloxy)-octan-2-one (8):

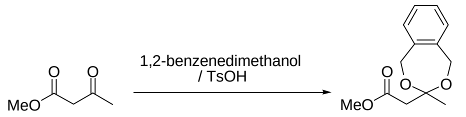


To a solution of hydroxyketone **7** (25.02 g, 96.07 mmol, 1.0 equiv) and *N,N*-

diisopropylethylamine (31 mL, 180 mmol, 1.9 equiv) in CH_2Cl_2 (230 mL) was added chloromethyl methyl ether (11 mL, 150 mmol, 1.5 equiv) slowly by syringe. The resulting solution was stirred for 10 min at room temperature then at a gentle reflux for 18 h. The reaction was cooled to room temperature and quenched by the addition of saturated sodium bicarbonate (50 mL). After dilution with pentane (250 mL), the phases were separated and the organic phase washed with saturated sodium bicarbonate (2x). The combined aqueous phases were back extracted with pentane (3x), and the combined organic phases were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography (8:1 hexanes/*tert*-butyl methyl ether then 1:1 hexanes/*tert*-butyl methyl ether) to provide 16.39 g of the desired product **8** as well as some impure material. This material was rechromatographed (10:1 hexanes/*tert*-butyl methyl ether then 1:1 hexanes/*tert*-butyl methyl ether) to provide a total yield of 21.39 g (70.25 mmol, 73%) of the desired **8** as a clear, colorless oil.

R_f: 0.65 (2:1 hexanes/*tert*-butyl methyl ether). $[\alpha]_D$ = -26.0 (*c* 0.93, CH_2Cl_2). IR: 2956, 2896, 2819, 1720, 1358, 1253 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.62 (A of AB, J = 7 Hz, 1H), 4.59 (B of AB, J = 7 Hz, 1H), 4.03 (ddd, J = 9, 5, 3 Hz, 1H), 3.29 (s, 3H), 3.26-3.29 (m, 1H), 2.68 (dd, J = 16, 9 Hz, 1H), 2.29 (dd, J = 16, 3 Hz, 1H), 2.16 (s, 3H), 1.91-1.98 (m, 1H), 1.62-1.71 (m, 1H), 0.84-0.88 (m, 9H), 0.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.3, 96.3, 78.7, 75.7, 55.6, 44.8, 39.2, 31.3, 31.1, 20.2, 16.7, 10.7, 0.9. Anal. calcd. for $C_{15}H_{32}O_4Si$: C 59.17, H 10.59. Found: C 58.97, H 10.20.

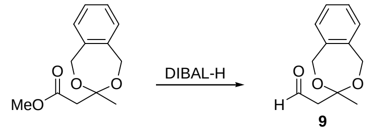
Methyl 2-(7-Methyl-5,9-dihydro-6,8-dioxa-benzocyclohepten-7-yl)acetate



To a solution of 1,2-benzenedimethanol (43.36 g, 313.8 mmol, 1.0 equiv) and methyl acetoacetate (55.17 g, 475.1 mmol, 1.5 equiv) in benzene (600 mL) was added *p*-toluene sulfonic acid hydrate (3.05 g, 16 mmol, 0.05 equiv). The resulting mixture was heated at reflux for 1 h with azeotropic removal of water by a Dean-Stark trap. After cooling to room temperature, the reaction mixture was diluted with *tert*-butyl methyl ether (500 mL) and washed with 1M sodium hydroxide (2x) and brine. The organic phase was dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography (5:1 hexanes/ethyl acetate) to provide the ketal-ester as a yellow oil (47.31 g, 200.2 mmol, 64%).

R_f: 0.56 (3:1 hexanes/ethyl acetate). IR: 2995, 2950, 2863, 1742 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14-7.18 (m, 2H), 7.03-7.07 (m, 2H), 4.88 (A of AB, J = 15 Hz, 1H), 4.86 (B of AB, J = 15 Hz, 1H), 3.71 (s, 3H), 2.86 (s, 2H), 1.63 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9, 137.6, 126.8, 126.1, 101.9, 65.0, 51.9, 42.1, 21.9. Anal. calcd. for $C_{13}H_{16}O_4$: C 66.09, H 6.83. Found: C 66.16, H 6.69.

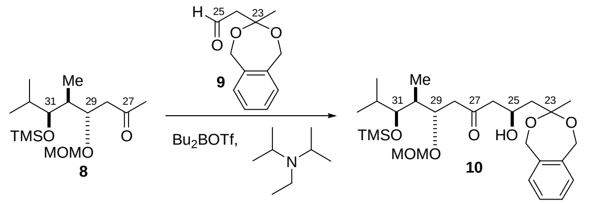
(7-Methyl-5,9-dihydro-6,8-dioxa-benzocyclohepten-7-yl)-acetaldehyde (9):



To a cooled (-78 °C) solution of the ketal-ester (46.96 g, 198.8 mmol, 1.0 equiv) in ether (760 mL) was added diisobutylaluminum hydride (294 mL, 0.99 M in hexanes, 1.5 equiv) by cannula down the side of the flask over 20 min. The reaction was stirred for 30 min at –78 °C then quenched by the addition of dry acetone (20 mL) and removed from the cold bath. Saturated potassium sodium tartrate (750 mL) was added and the mixture was stirred vigorously with a mechanical stirrer for 12 h at room temperature. The phases were separated and the aqueous phase extracted with ether (2x). The organic phases were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography twice (8:1 CH_2Cl_2/hexanes then 10:1 to 7:1 hexanes/*tert*-butyl methyl ether) to provide the known aldehyde[5] (**9**) as a clear, colorless oil (16.54 g, 80.20 mmol, 40%).

R_f: 0.17 (7:1 hexanes/*tert*-butyl methyl ether). IR: 3061, 3022, 2995, 2940, 2863, 2742, 1726, 1451, 1380 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$,): δ 9.77 (t, J = 3 Hz, 1H), 7.17-7.21 (m, 2H), 7.05-7.09 (m, 2H), 4.89 (s, 4H), 2.84 (d, J = 3, 2H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.3, 137.4, 126.9, 126.2, 101.5, 65.0, 50.4, 22.6. Anal. calcd. for $C_{12}H_{14}O_3$: C 69.89, H 6.84. Found: C 69.51, H 6.69.

β-Hydroxy ketone (10):



To a cooled (-78 °C) solution of ketone **8** (20.90 g, 68.64 mmol, 1.0 equiv) in ether (660 mL) was added *N,N*-diisopropylethylamine (14 mL, 80 mmol, 1.2 equiv) followed by dibutylboron triflate (74 mL, 1.0 M in CH_2Cl_2, 74 mmol, 1.1 equiv) by cannula over 9 min, resulting in the formation of a white precipitate. The resulting mixture was stirred for 30 min at –78 °C then cooled to –100 °C. To this mixture was added a solution of aldehyde **9** (16.41 g, 79.57 mmol, 1.16 equiv) in ether (74 mL). The resulting mixture was stirred for 3 h at –100 °C then allowed to warm to –75 °C over 75 min. The reaction was quenched by addition of 6:1 MeOH/pH 7 buffer (490 mL), then warmed to 0 °C and treated with 2:1 MeOH/30% aqueous H_2O_2 (210 mL). The ice bath was then removed and the reaction was stirred for 1 h, then diluted with brine and pH 7 buffer. The aqueous phase was saturated with solid sodium chloride and phases separated. The aqueous phase was extracted with ether (3x) and the combined organic phases washed with 1:1 1M sodium hydroxide/brine (2x) and brine. The combined organics were dried over magnesium sulfate, filtered through celite, and concentrated

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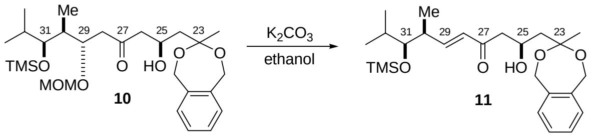
[5] H. Watanabe, K. Mori, *J. Chem. Soc. Perkin Trans. 1* **1991**, 2919-2934.

under reduced pressure. ^{1}H NMR analysis of the crude product revealed a diastereomeric ratio of 4:1.

The crude product was purified by repeated flash chromatography as follows: Initial chromatography (2:1 then 1:1 hexanes/*tert*-butyl methyl ether) afforded the desired alcohol **10** ("batch 1," 16.66 g), a 5:1 diastereomeric mixture of **10** and the C25 epimer ("batch 2", 4.99 g), and two impure batches of material ("batch 3" containing a higher R_f impurity and "batch 4" containing a 1:2 diastereomeric mixture of **10** and the C25 epimer as well as lower R_f impurities). "Batch 2" was rechromatographed (15:1 then 10:1 CH_2Cl_2 / ethyl acetate) to afford the desired diastereomer **10** (2.10 g). "Batch 3" was rechromatographed (8:1 then 5:1 toluene/ethyl acetate) to provide the desired diastereomer **10** (1.02 g). "Batch 4" was rechromatographed (10:1 then 5:1 CH_2Cl_2/ethyl acetate) to provide a 6:1 diastereomeric mixture of **10** and the C25 epimer (5.83 g) and some impure material that was rechromatographed (2:1 hexanes/*tert*-butyl methyl ether) to provide the desired alcohol **10** (1.25 g). The yield of both diastereomers was 29.75 g (58.25 mmol, 85%) from which 21.04 g of the desired **10** could be isolated (41.19 mmol, 60%).

R_f: major diastereomer = 0.27 minor diastereomer = 0.21 (10:1 CH_2Cl_2/ethyl acetate). R_f: major diastereomer = 0.42 minor diastereomer = 0.35 (1:1 hexanes/*tert*-butyl methyl ether). $[\alpha]_D$ = -8.9 (*c* 0.823, CH_2Cl_2). IR: 3516, 3061, 2962, 2824, 1709 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15-7.19 (m, 2H), 7.03-7.07 (m, 2H), 4.92 (A of AB, J = 15 Hz, 2H), 4.84 (B of AB, J = 15 Hz, 1H), 4.78 (B of AB, J = 15 Hz, 1H), 4.63 (A of AB, J = 7 Hz, 1H), 4.60 (B of AB, J = 7 Hz, 1H), 4.35-4.42 (m, 1H), 4.07 (ddd, J = 9, 5, 2 Hz, 1H), 3.51 (d, J = 2 Hz, 1H), 3.30 (s, 3H), 3.29 (dd, J = 6, 4 Hz, 1H), 2.71 (dd, J = 17, 9 Hz, 1H), 2.71 (dd, J = 17, 8 Hz, 1H), 2.58 (dd, J = 17, 5 Hz, 1H), 2.33 (dd, J = 17, 2 Hz, 1H), 2.07 (dd, J = 14, 9 Hz, 1H), 1.91-1.98 (m, 1H), 1.81 (dd, J = 14, 3 Hz, 1H), 1.63-1.72 (m, 1H), 1.56 (s, 3H), 0.82-0.84 (m, 9H), 0.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.6, 137.8, 137.5, 126.8, 126.8, 126.1, 126.1, 103.7, 96.4, 78.7, 75.4, 65.0, 64.8, 64.6, 55.6, 51.0, 45.0, 42.5, 39.3, 31.3, 21.5, 20.2, 16.7, 10.7, 0.9. Anal. calcd. for $C_{27}H_{46}O_7Si$: C 63.50, H 9.08. Found: C 63.53, H 8.69.

β-Hydroxyenone (11):

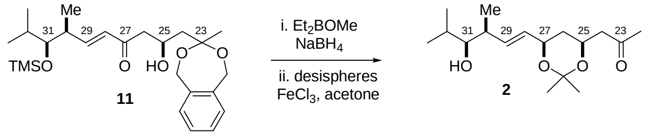


To a cooled (0 °C) solution of **10** (19.92 g, 39.00 mmol, 1.0 equiv) in ethanol (95%, 390 mL) was added aqueous potassium carbonate (78 mL, 0.10 M, 7.8 mmol, 0.2 equiv). The resulting mixture was stirred for 1.5 h at 0 °C then allowed to warm to 13 °C over 3 h. The reaction mixture was then diluted with hexanes (400 mL) and *tert*-butyl methyl ether (400 mL), dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography to provide the desired enone **11** as a clear, faintly colored oil (14.11 g, 31.45 mmol, 81%).

R_f: 0.60 (2:1 hexanes/ethyl acetate). $[\alpha]_D$ = -8.3 (*c* 0.621, CH_2Cl_2). IR: 3511, 3064, 3017, 2959, 2872, 1691, 1668, 1621 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14-

7.18 (m, 2H), 7.03-7.07 (m, 2H), 6.79 (dd, J = 16, 8 Hz, 1H), 6.09 (dd, J = 16, 1 Hz, 1H), 4.93 (A of AB, J = 15 Hz, 2H), 4.84 (B of AB, J = 15 Hz, 1H), 4.78 (B of AB, J = 15 Hz, 1H), 4.38-4.45 (m, 1H), 3.58 (d, J = 2 Hz, 1H), 3.32 (dd, J = 6, 5 Hz, 1H), 2.83 (dd, J = 17, 7 Hz, 1H), 2.69 (dd, J = 17, 5 Hz, 1H), 2.44-2.52 (m, 1H), 2.09 (dd, J = 14, 9 Hz, 1H), 1.85 (dd, J = 14, 3 Hz, 1H), 1.61-1.1.70 (m, 1H), 1.57 (s, 3H), 1.03 (d, J = 7 Hz, 3H), 0.86 (d, J = 7 Hz, 3H), 0.82 (d, J = 7 Hz, 3H), 0.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 151.7, 137.8, 137.5, 129.6, 126.8, 126.1, 103.7, 80.9, 65.1, 65.0, 64.7, 47.2, 42.5, 41.0, 31.6, 21.5, 20.4, 17.1, 15.0, 0.8. Anal. calcd. for $C_{25}H_{40}O_5Si$: C 66.93, H 8.99. Found: C 66.92, H 8.60.

C22-C33 fragment (2):

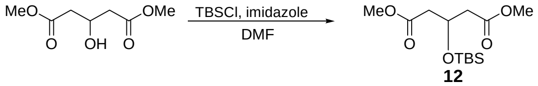


To a cooled (-78 °C) solution of hydroxyketone **11** (14.0 g, 31.2 mmol, 1.0 equiv) in THF (383 mL) and methanol (95 mL) was added diethylmethoxyborane (37 mL, 1.0 M in THF, 37 mmol, 1.2 equiv). The resulting solution was stirred for 15 min at -78 °C, then sodium borohydride (2.0 g, 53 mmol, 1.7 equiv) was added in one portion. The reaction was then stirred for 1 h at -78 °C and allowed to warm to room temperature over 70 min. The reaction was quenched with saturated potassium sodium tartrate (250 mL) and stirred vigorously for 2 h with a mechanical stirrer. The mixture was then diluted with water (250 mL) and the phases separated. The aqueous phase was back extracted with *tert*-butyl methyl ether (4x). The organics were combined, and a new aqueous phase separated which was saturated with solid sodium chloride and separated. This aqueous phase was then back extracted with *tert*-butyl methyl (2x). The combined organic extracts were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. ^{1}H NMR of the crude material revealed the presence of some broad peaks indicative of the presence of borate impurities, so the crude material was taken up in 300 mL methanol and then methanol was distilled off under atmospheric pressure. This effectively removed the remaining boron as trimethyl borate but also resulted in substantial cleavage of the TMS ether and partial cleavage of the benzodioxepine. This mixture was, therefore, not purified, and was used directly in the next reaction as described below.

To a solution of the crude material prepared as described above in acetone (200 mL) was added desispheres (17.2 g). The resulting mixture was cooled to -13 °C and a solution of ferric chloride in acetone (117 mL, 0.26 M, 31 mmol, 1 equiv based on **11**, pre-dried with desispheres) was added over 3 min using a pressure-equalizing addition funnel containing 1 g desispheres. The resulting mixture was stirred for 1 h, then allowed to warm to -6 °C and quenched by addition of triethylamine (7 mL) followed by potassium carbonate (20% aqueous, 150 mL). The mixture was diluted with *tert*-butyl methyl ether (1 L) and the phases separated. The organic phase was washed with brine (2x), dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography (1.25:1 hexanes/*tert*-butyl methyl ether) to provide the desired ketone **2** as a clear, light yellow oil (6.32 g, 21.2 mmol, 68% from **11**).

R_f: 0.31 (2:1 hexanes/ethyl acetate). $[\alpha]_D$ = - 5.1 (*c* 0.847, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ 5.61 (ddd, J = 16, 7, 1 Hz, 1H), 5.45 (ddd, J = 16, 6, 1 Hz, 1H), 4.30-4.36 (m, 2H), 3.12 (q, J = 6, 1H), 2.67 (dd, J = 16, 7 Hz, 1H), 2.43 (dd, J = 16, 6 Hz, 1H), 2.28-2.35 (m, 1H), 2.15 (s, 3H), 1.64-1.72 (m, 1H), 1.57 (dt, J = 13, 3 Hz, 1H), 1.45 (s, 3H), 1.36 (s, 3H), 1.18-1.26 (m, 1H), 0.99 (d, J = 7 Hz, 3H), 0.89 (d, J = 7 Hz, 3H), 0.87 (d, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 135.2, 130.6, 98.8, 79.7, 69.8, 65.3, 50.0, 39.3, 37.0, 31.1, 30.5, 30.1, 19.7, 19.7, 17.0, 13.9. Anal. calcd. for $C_{17}H_{30}O_4$: C 68.42, 10.13. Found: C 68.25, H 9.75.

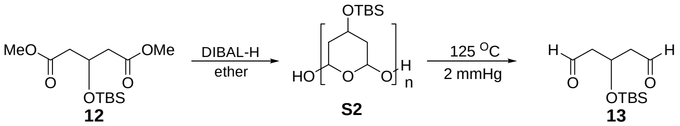
3-(*tert*-Butyl-dimethyl-silanyloxy)-pentanedioic acid dimethyl ester (12):



To a cooled (0 °C) solution of dimethyl 3-hydroxygluterate (10.44 g, 59.26 mmol, 1.0 equiv) and imidazole (5.23 g, 76.8 mmol, 1.3 equiv) in *N,N*-dimethylformamide (20 mL) was added *tert*-butyldimethylsilyl chloride (9.4 g, 62 mmol, 1.1 equiv) in one portion. The reaction was allowed to stir for 14 h at 0 °C, then warmed to room temperature and diluted with ether (100 mL). The reaction was then washed with water and brine (2x), and the combined aqueous phases were back-extracted with ether. The combined organics were dried over magnesium sulfate and concentrated under reduced pressure. The crude was directly distilled under reduced pressure (*ca.* 1 mm Hg, b.p.= 113-121 °C, lit. 114-116 °C at 0.8 mm Hg) to afford the known[6] diester **12** (14.40 g, 49.56 mmol, 84%).

^1H NMR (500 MHz, $CDCl_3$): δ 4.53 (pentet, J = 6 Hz, 1H), 3.65 (s, 6H), 2.49-2.58 (m, 4H), 0.82 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.4, 66.3, 51.6, 42.4, 25.6, 17.8, -5.0.

3-(*tert*-Butyl-dimethyl-silanyloxy)-pentanedial (13):



To a cooled (-78 °C) solution of ester **12** (18.0 g, 62.0 mmol, 1.0 equiv) in ether (284 mL) was added diisobutylaluminum hydride (139 mL, 1.0 M in hexanes, 140 mmol, 2.2 equiv) slowly via a pressure-equalizing addition funnel over 50 min. The solution was stirred for 1 h at -78 °C then quenched by the addition of dry acetone (3 mL) followed by saturated potassium sodium tartrate (250 mL). The mixture was stirred vigorously for 75 min at room temperature, and another portion of saturated potassium sodium tartrate (100 mL) was added. After an additional 105 min, the phases were separated, and the aqueous phase was extracted with ether (6x). The combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. This product provided NMR spectra which displayed broad, nondescript signals and is likely a hydrated, cyclic, polymeric material (**S2**). It was dehydrated and depolymerized

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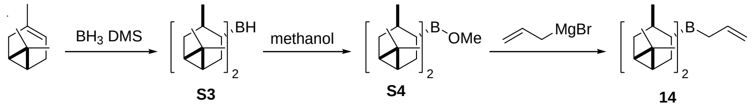
[6] L. Nová, J. Roháty, L. Poppe, G. Hornyánsqky, P. Kolonits, I. Zelei, I. Fehér, J. Fekete, É. Szabó, U. Záhorsky, A. Jávor, C. Szántay, *Liebigs Ann. Chem.* **1992**, 145-147.

prior to use by heating in a sand bath at 125 °C for 40 min under vacuum (*ca*. 2 mm Hg). This provides the largely monomeric dialdehyde **13**[7] as a red oil which was used without further purification. Upon prolonged exposure to the atmosphere, compound **13** undergoes reversible partial hydration and polymerization and must be dehydrated in order to reform the dialdehyde.

^{1}H NMR (500 MHz, CDCl$_3$): δ 9.77 (t, J = 2 Hz, 2H), 4.70 (pentet, J = 6 Hz, 1H), 2.60-2.70 (m, 4H), 0.83 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 200.6, 63.4, 51.0, 25.6, 17.9, -4.7.

4-^{d}Icr$_2$B-All (14):

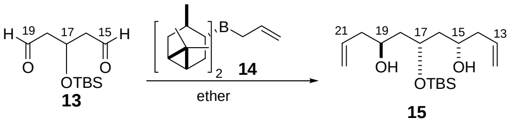


To a cooled (0 °C) solution of (1S)-(+)-3-carene (79.74 g, 585.3 mmol, 2.4 equiv) in THF (210 mL) was added borane dimethylsulfide (24 mL, 10M, 240 mmol, 1.0 equiv) portionwise by cannula. The solution was stirred for 2 min then held at 0 °C without stirring for 24 h, during which time a white crystalline solid precipitated. After warming to room temperature, THF was removed by cannula. The solids were washed with dry pentane (2x), and these washings were also removed by cannula. Drying under vacuum (*ca*. 2 mm Hg) for 90 min afforded **S3** as a white solid (47.83 g, 167.1 mmol, 70%).

These solids prepared above were suspended in ether (118 mL) and cooled to 0 °C. Anhydrous methanol (8.1 mL, 200 mmol, 1.2 equiv) was then added via cannula over 22 min, and the reaction stirred for 1 h at 0 °C then allowed to warm to room temperature over 1 h, after which time hydrogen gas evolution had ceased. A distillation apparatus was attached to the reaction flask with N$_2$ out gassing, and the reaction and receiving flask were cooled to –78 °C. The system was then placed under vacuum (*ca*. 2 mm Hg) and allowed to warm to room temperature with stirring as the solvents were removed by distillation and collected in the cold receiving flask. The resulting clear, colorless oil (**S4**) was stirred for an additional 1 h at room temperature under vacuum to remove any remaining traces of solvent.

After equipping the flask with a pressure-equalizing addition funnel, this oil was dissolved in ether (148 mL) and the resulting solution cooled to 0 °C. Allylmagnesium bromide (153 mL, 0.98 M in ether, 150 mmol, 0.90 equiv) was added dropwise via the addition funnel over 60 min with vigorous stirring. The funnel was washed with ether (2x) and the heterogeneous mixture allowed to warm to room temperature and stir for 105 min. This mixture was used directly in the next step.

6-(*tert*-Butyl-dimethyl-silanoxy)-undeca-1,10-diene-4,8-diol (15):



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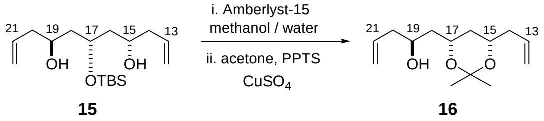
[7] S. L. Buckley, M. G. B. Drew, L. M. Harwood, A. J. Macías-Sánchez, *Tetrahedron Lett.* **2002**, *43*, 3593-3596.

To the cooled (-78 °C) heterogeneous mixture containing **14** (11.38 g, 150 mmol, 2.4 equiv) was added a solution of dialdehyde **13** (14.28 g, 62 mmol, 1.0 equiv) in ether (45 mL) dropwise via pressure-equalizing addition funnel over 30 min. The mixture was stirred for 2 h at -78 °C then quenched by the addition of dry methanol (3 mL) and allowed to warm to 0 °C. Aqueous sodium hydroxide (3 M, 60 mL) was then added via addition funnel, followed by hydrogen peroxide (30 % aqueous, 120 mL). The biphasic mixture was heated to reflux for 9 h then diluted with 100 mL water and the phases separated. The aqueous phase was back extracted with ether (5x) then saturated with sodium chloride and extracted again with ether. The combined organic extrtacts were washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude product was purified by flash chromatography (5:1 hexanes/ethyl acetate then 2.5:1 hexanes/ethyl acetate) to provide diol **15** (10.31 g, 32.78 mmol, 53% over 2 steps, >98% ee, 10:1 dr) as a faintly colored oil.

R_f: 0.37 (2:1 hexanes/ethyl acetate). $[\alpha]_D$ = +13.0 (*c* 0.483, CH_2Cl_2). IR: 3407, 3077, 2956, 2929, 2857, 1638, 1248 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.74-5.85 (m, 2H), 5.06-5.15 (m, 4H), 4.21 (dddd, J = 7, 7, 5, 5 Hz, 1H), 3.89-3.96 (m, 1H), 3.66-3.73 (m, 1H), 3.18 (br s, 1H), 2.13-2.28 (m, 5H), 1.62-1.76 (m, 4H), 0.88 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.7, 134.4, 118.2, 117.6, 69.8, 68.3, 67.7, 42.8, 42.5, 42.4, 41.4, 25.8, 17.8, -4.6, -4.7. Anal. calcd. for $C_{17}H_{34}O_3Si$: C 64.92, H 10.89. Found: C 64.64, H 10.58.

1-(6-Allyl-2,2-dimethyl-[1,3]dioxin-4-yl)-pent-4-en-2-ol (16):

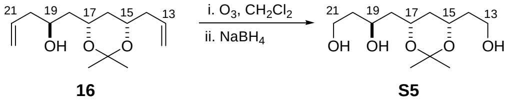


To a solution of diol **15** (10.00 g, 31.79 mmol, 1.0 equiv) in methanol (100 mL) and water (20 mL) was added Amberlyst-15 resin (6.0 g). The resulting mixture was stirred for 4.5 h then quenched by the addition of triethylamine (10 mL) and filtered through celite and washed with ethyl acetate. The organics were concentrated under reduced pressure to give the crude triol as a viscous, amber-colored oil that was used directly without further purification.

To a solution of the crude triol prepared above in acetone (489 mL) was added anhydrous copper (II) sulfate (51.70 g, 323.9 mmol, 10 equiv) and pyridinium *p*-toluenesulfonate (0.40 g, 1.6 mmol, 0.050 equiv). The resulting mixture was stirred for 4.5 h then filtered through a short plug of silica over a pad of celite and washed with acetone. The filtrate was concentrated under reduced pressure to give acetonide **16** as a yellow oil which was used without further purification. A purified sample of acetonide **16** provided the following spectral characteristics:

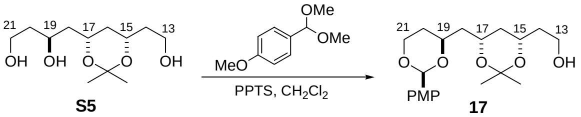
R_f: 0.24 (5:1 hexanes/ethyl acetate). $[\alpha]_D$ = +17.2 (*c* 0.501, CH_2Cl_2). IR: 3448, 3075, 2994, 2936, 2907, 1645 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 5.81 (dddd, J = 17, 10, 7, 7 Hz, 1H), 5.77 (dddd, J = 17, 10, 7, 7 Hz, 1H), 5.05-5.12 (m, 4H), 4.13-4.20 (m, 1H), 3.84-3.96 (m, 2H), 2.74 (d, J = 4 Hz, 1H), 2.26-2.32 (m, 1H), 2.18-2.24 (m, 2H), 2.10-2.17 (m, 1H), 1.58-1.63 (m, 2H), 1.43 (s, 3H), 1.40-1.45 (m, 1H), 1.37 (s, 3H), 1.25-1.33 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.0, 134.0, 117.6, 117.2, 98.7, 68.6, 67.5, 67.0, 42.0, 41.6, 40.7, 35.9, 30.2, 19.7. Anal. calcd. for $C_{14}H_{24}O_3$: C 69.96, H 10.06. Found: C 69.58, H 10.08.

4-[6-(2-Hydroxy-ethyl)-2,2-dimethyl-[1,3]dioxin-4-yl]-butane-1,3-diol:



To a solution of the crude acetonide **16** prepared as described above in CH_2Cl_2 (228 mL) was added solid potassium carbonate (8.8 g, 64 mmol, 2.0 equiv). The reaction mixture was cooled to -78 °C, and methanol (60 mL) was added by cannula. Ozone was then bubbled into this mixture until a blue color persisted, and the excess ozone was then purged with N_2. The reaction was warmed to 0 °C, and sodium borohydride (4.8 g, 130 mmol, 4.0 equiv) was added in two portions. The mixture was stirred at 0 °C for 1 h then allowed to warm to room temperature and stirred for 12 h. An additional portion of sodium borohydride (2.4 g, 63 mmol, 2.0 equiv) was added, and the mixture stirred for 1.5 h. The reaction was then quenched by the addition of excess solid ammonium chloride (95 g) and stirred for 2.5 h. This mixture was filtered through celite and washed with 2:1 ethyl acetate/methanol, then concentrated under reduced pressure to give a cloudy, viscous residue indicative of incomplete borate methanolysis. The residue was dissolved in methanol (500 mL) and solid ammonium chloride (20 g) was added. About 250 mL of the methanol was removed by distillation in order to remove the volatile trimethylborate, and the residue was taken up in ethyl acetate, filtered through celite, and concentrated under reduced pressure. The product was subjected to filtration through a short silica gel column, (15:1 then 10:1 ethyl acetate/methanol) to remove polar impurities, and then taken on to the next step crude.

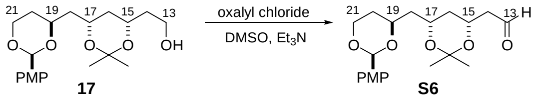
2-{6-[4-Methoxy-phenyl)-[1,3]dioxin-4-ylmethyl]-2,2-dimethyl-[1,3]dioxin-4-yl}-ethanol (17):



To a cooled (0 °C) solution of **S5** in CH_2Cl_2 (175 mL) was added *p*-anisaldehyde dimethyl acetal (4.8 mL, 28 mmol, 0.9 equiv.) by syringe and pyridinium *p*-toluenesulfonate (1.38 g, 5.5 mmol, 0.2 equiv). The reaction was stirred for 1 h at 0 °C, then filtered through a short plug of silica over a pad of celite, washed with ether, and concentrated under reduced pressure. Flash chromatography (1:1.5 hexanes/ethyl acetate) provided analytically pure alcohol **17** as a very viscous, light-yellow oil (8.56 g, 23.360 mmol, 73 % over 4 steps).

R_f: 0.64 (ethyl acetate). $[\alpha]_D = +59.8$ (*c* 0.6945, CH_2Cl_2). IR: 3436, 3000, 2936, 2912, 2866 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35-7.39 (m, 2H), 6.84-6.89 (m, 2H), 5.46 (s, 1H), 4.15-4.25 (m, 2H), 4.02-4.13 (m, 2H), 3.96 (ddd, J = 12, 12, 2Hz, 1H), 3.78 (s, 3H), 3.70-3.3.78 (m, 2H), 2.54 (br s, 1H), 1.54-1.81 (m, 5H), 1.45 (s, 3H), 1.45-1.50 (m, 1H), 1.42 (dt, J = 13, 2 Hz, 1H), 1.38 (s, 3H). 1.25-1.33 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 131.4, 127.1, 113.6, 100.8, 98.7, 73.0, 69.7, 67.0, 64.7, 61.0, 55.3, 42.8, 38.0, 37.1, 31.7, 30.3, 20.0. Anal. calcd. for $C_{20}H_{30}O_6$: C 65.55, H 8.25. Found: C 65.18, H 7.93.

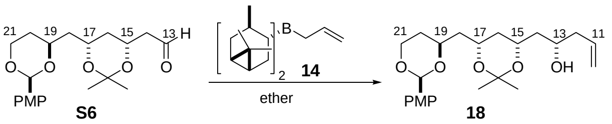
2-{6-[4-Methoxy-phenyl)-[1,3]dioxin-4-ylmethyl]-2,2-dimethyl-[1,3]dioxin-4-yl}-acetaldehyde:



To a cooled (-78 °C) solution of oxalyl chloride (3.0 mL, 34 mmol, 1.5 equiv) in CH_2Cl_2 (183 mL) was added DMSO (3.3 mL, 47 mmol, 2.0 equiv) dropwise by syringe. The reaction was stirred for 20 min at -78 °C, then a solution of alcohol **17** (8.49 g, 23.18 mmol, 1.0 equiv) in CH_2Cl_2 (55 mL) was added dropwise by cannula over 25 min. The flask was washed with CH_2Cl_2 (2 mL), which was also added by cannula. The cloudy mixture was stirred for 30 min at -78 °C after which triethylamine (12.9 mL, 92.6 mmol, 4.0 equiv) added slowly by syringe. The reaction was then stirred for a few minutes at -78 C, then the cold bath was removed, and the reaction was stirred for 1 hour at which point it was at room temperature. The reaction was quenched by the addition of saturated ammonium chloride (100 mL), and the phases were separated and the aqueous phase back extracted with CH_2Cl_2 (4 x). The combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. Flash chromatography (9:1 dichloromethane/ethyl acetate) provided **S6** (7.91 g, 21.71 mmol, 94 %) as an oil.

R_f: 0.23 (3:1 hexanes/ethyl acetate). $[\alpha]_D = +73.8$ (*c* 0.6295, CH_2Cl_2). IR: 2995, 2945, 2912, 2841, 2726, 1726, 1616, 1517 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.75 (br t, J = 2 Hz, 1H), 7.35-7.39 (m, 2H), 6.84-6.89 (m, 2H), 5.46 (s, 1H), 4.38 (dddd, J = 12, 7, 5, 2 Hz, 1H), 4.17-4.25 (m, 2H), 4.05 (dddd, J = 12, 9, 3, 3 Hz, 1H), 3.94 (ddd, J = 12, 12, 2 Hz, 1H), 3.78 (s, 3H), 2.57 (ddd, J = 17, 7, 2 Hz, 1H), 2.44 (ddd, J = 17, 5, 2 Hz, 1H), 1.72-1.81 (m, 1H), 1.56-1.63 (m, 2H), 1.53 (dt, J = 13, 2 Hz, 1H), 1.45 (s, 3H), 1.44-1.50 (m, 1H), 1.37 (s, 3H), 1.18-1.27 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.0, 159.8, 131.4, 127.1, 113.6, 100.8, 98.9, 72.9, 66.9, 64.7, 64.6, 55.3, 49.8, 42.8, 37.0, 31.7, 30.1, 19.8. Anal. calcd. for $C_{20}H_{28}O_6$: C 65.92, H 7.74. Found: C 65.64, H 7.69.

1-{6-[2-(4-Methoxy-phenyl)-[1,3]dioxin-4-ylmethyl]-2,2-dimethyl-[1,3]dioxin-4-yl}-pent-4-en-2-ol (18):

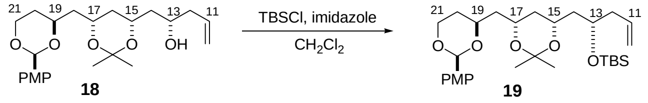


To a cooled (-100 °C) mixture containing **14** (26 mmol, 1.4 equiv, prepared as described above) in ether (49 mL) was added aldehyde **S6** (7.03 g, 19.29 mmol, 1.0 equiv) in ether (20 mL) dropwise by cannula over 10 min. The flask was rinsed with ether (3 mL) and also added by cannula. The reaction was stirred for 1 h at –100 °C then allowed to warm to –78 °C over a period of 30 min, and stirred for an additional 45 min at that temperature. The reaction was then quenched by the addition of dry methanol (1 mL) then placed in an ice bath and allowed to warm to 0 °C. Sodium hydroxide (3M, 15 mL), hydrogen peroxide (30 % aqueous, 30 mL), and ethanol (10 mL) were then added sequentially, and the ice bath was removed and the resulting mixture was stirred for 9 h.

The solution was then heated to reflux for 5 h, at which point TLC analysis suggested incomplete hydrolysis, therefore THF (40 mL) and aqueous sodium hydroxide (3M, 15 mL) were added and the mixture was again heated at reflux for 4.5 h. TLC analysis now showed substantial improvement with well defined spots, and the reaction was saturated with solid sodium chloride and the phases separated. The aqueous phase was extracted with ether (5 x 50 mL), and the combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. ^{1}H NMR analysis of the crude material revealed a diastereomeric ration of $\geq$ 30:1. Flash chromatography (3:1 hexanes/ethyl acetate) provided the homoallylic alcohol (**18**) as a colorless, viscous oil (6.79 g, 16.7 mmol, 87 %).

R_f: 0.30 (2:1 hexanes/ethyl acetate). $[\alpha]_D$ = +47.1 (*c* 0.456, CH_2Cl_2). IR: 3523, 3075, 2988, 2941, 2906, 2837, 1639, 1621, 1583, 1516 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ 7.63-7.67 (m, 2H), 6.84-6.88 (m, 2H), 5.95 (dddd, J = 17, 10, 7, 7 Hz, 1H), 5.06-5.11 (m, 2H), 4.06 (dddd, J = 12, 9, 3, 3 Hz, 1H), 3.94-4.01 (m, 2H), 3.78-3.84 (m, 1H), 3.68 (dddd, J = 12, 9, 3, 3 Hz, 1H), 3.55 (ddd, J = 12, 12, 2 Hz, 1H), 3.24 (s, 3H), 3.18 (s, 1H), 2.28-2.35 (m, 1H), 2.16-2.23 (m, 1H), 1.43-1.65 (m, 5H), 1.40 (s, 3H), 1.28 (s, 3H), 1.27-1.32 (m, 1H), 1.02-1.10 (m, 1H), 0.90-0.95 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6): δ 160.8, 136.1, 132.9, 128.2, 117.4, 114.1, 101.9, 99.1, 73.3, 71.2, 70.6, 67.3, 65.2, 55.1, 43.8, 43.2, 43.0, 38.3, 32.5, 30.8, 20.4. Anal. calcd. for $C_{23}H_{34}O_6$: C 67.96, H 8.43. Found: C 67.60, H 8.59.

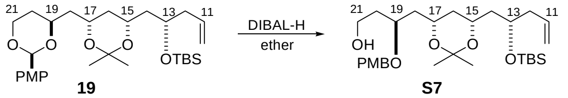
***tert*-Butyl-(1-{6-[2-(4-methoxy-phenyl)-[1,3]dioxan-4-ylmethyl]-2,2-dimethyl-[1,3]dioxan-4-ylmethyl}-but-3-enyloxy)-dimethyl-silane (19):**



To a cooled (0 °C) solution of homoallylic alcohol **18** (6.74 g, 16.6 mmol, 1.0 equiv) and imidazole (2.31 g, 33.9 mmol, 2.0 equiv) in CH_2Cl_2 (33 mL) was added *tert*-butyldimethylsilyl chloride (3.79 g, 25.1 mmol, 1.5 equiv) in one portion. The reaction was allowed to warm to room temperature and then stirred for 18.5 h. The reaction was then diluted with ether (100 mL) and washed with saturated ammonium chloride (2 x). The aqueous phase was extracted with ether (5 x), and the combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. Flash chromatography (10:1 hexanes/ethyl acetate) using a small silica column provided **19** contaminated with *tert*-butyldimethylsilanol. Azeotropic removal of the silanol with toluene provided analytically pure **19** as a viscous faintly colored oil (8.47 g, 16.3 mmol, 98 %).

R_f: 0.24 (10:1 hexanes/ethyl acetate). $[\alpha]_D$ = +49.5 (*c* 0.672, CH_2Cl_2). IR: 3075, 2989, 2953, 2852, 1639, 1616, 1586, 1517 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ 7.36-7.40 (m, 2H), 6.85-6.89 (m, 2H), 5.74-5.83 (m, 1H), 5.47 (s, 1H), 4.98-5.04 (m, 2H), 4.22 (br dd, J = 12, 4 Hz, 1H), 4.13 (dddd, J = 12, 9, 3, 3 Hz, 1H), 4.05 (dddd, J = 12, 9, 3, 3 Hz, 1H), 3.91-4.01 (m, 2H), 3.82 (pentet, J = 6 Hz, 1H), 3.78 (s, 3H), 2.13-2.28 (m, 2H), 1.72-1.82 (m, 1H), 1.64-1.71 (m, 2H), 1.56-1.62 (m, 1H), 1.45-1.52 (m, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.08-1.16 (m, 1H), 0.85 (s, 9H), 0.02 (s, 3 H), 0.00 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 159.7, 135.1, 131.4, 127.1, 117.0, 113.5, 100.7, 98.4, 73.2, 68.5, 67.0, 66.0, 64.9, 55.3, 43.3, 43.0, 41.7, 37.7, 31.8, 30.3, 25.8, 19.8, 18.0, -4.3, -4.6. Anal. calcd. for $C_{29}H_{48}O_6Si$: C 66.88, H 9.29. Found: C 66.69, H 9.37.

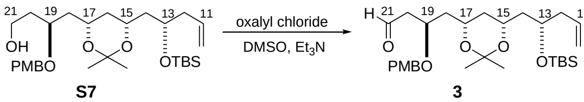
4-{6-[2-(*tert*-Butyl-dimethyl-silanyloxy)-pent-4-enyl]-2,2-dimethyl-[1,3]dioxan-4-yl}-3-(4-methoxy-benzyloxy)-butan-1-ol:



To a cooled (0 °C) solution of **19** (8.30 g, 15.9 mmol, 1.0 equiv) in CH_2Cl_2 (81 mL) was added diisobutylaluminum hydride (19 mL, 0.99 M in hexanes, 19 mmol, 1.2 equiv) portionwise by cannula (*note: If diisobutylaluminum hydride is added at room temperature desilylation of the C13 TBS group is observed).* The resulting solution was stirred for 10 min at 0 °C then allowed to warm to room temperature. After an additional 4 h, additional diisobutylaluminum hydride (3.2 mL, 0.99 M in hexanes, 3.2 mmol, 0.20 equiv) was added. The reaction was stirred for 30 min then quenched by addition of saturated potassium sodium tartrate (100 mL) and stirred vigorously for 2 h. The aqueous phase was saturated with solid sodium chloride and phases separated. The aqueous phase was extracted with 1:1 dichloromethane/ether (5 x). The combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. Flash chromatography (2.5:1 to 2:1 hexanes/ethyl acetate) provided alcohol **S7** (6.77 g, 12.95 mmol, 81 %).

R_f: 0.29 (2:1 hexanes/ethyl acetate). $[\alpha]_D = +21.6$ (*c* 0.8695, CH_2Cl_2). IR: 3451, 3072, 2989, 2929, 2857, 1637, 1610, 1588, 1517 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.22-7.26 (m, 2H), 6.84-6.87 (m, 2H), 5.74 (m, 1H), 4.99-5.04 (m, 2H), 4.49 (A of AB, J = 11 Hz, 1H), 4.45 (B of AB, J = 11 Hz, 1H), 3.95-4.06 (m, 2H), 3.78 (s, 3H), 3.66-3.88 (m, 4H), 2.35 (t, J = 5 Hz, 1H), 2.14-2.28 (m, 2H), 1.83-1.90 (m, 1H), 1.64-1.74 (m, 3H), 1.54-1.60 (m, 1H), 1.44-1.51 (m, 2H), 1.39 (s, 3H), 1.35 (s, 3H), 1.08-1.16 (m, 1H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 135.0, 130.4, 129.5, 117.0, 113.9, 98.4, 74.0, 71.6, 68.4, 66.0, 65.7, 60.1, 55.3, 43.3, 41.9, 41.8, 37.7, 36.4, 30.2, 25.8, 19.8, 18.0, -4.3, -4.6. Anal. calcd. for $C_{29}H_{50}O_6Si$: C 66.63, H 9.64. Found: C 66.31, H 9.73.

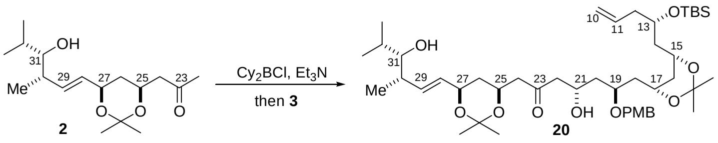
C10-C21 fragment (3):



To a cooled (-78 °C) solution of oxalyl chloride (1.6 mL, 18 mmol, 1.5 equiv) in CH_2Cl_2 (88 mL) was added DMSO (1.7 mL, 24 mmol, 2.0 equiv) dropwise by syringe. The resulting solution was stirred for 20 min at –78 °C, then a solution of **S7** (6.23 g, 11.99 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) was added dropwise by cannula over 14 min. The flask was rinsed with CH_2Cl_2 (1.5 mL), and this rinse was also added by cannula. After stirring 30 min at –78 °C, triethylamine (6.7 mL, 48 mmol, 4 equiv) was added dropwise by syringe. The reaction was then stirred for a few minutes at -78 C, then the cold bath was removed, and the reaction was stirred for 1 hour at which point it was at room temperature. The reaction was quenched by the addition of saturated ammonium chloride (50 mL), the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (4 x). The combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. Flash chromatography (7:1 to 5:1 hexanes/ethyl acetate) provided aldehyde **3** (5.28 g, 10.14 mmol, 85 %) as a viscous, light yellow oil.

R_f: 0.77 (2:1 hexanes/ethyl acetate). $[\alpha]_D = +28.0$ (*c* 1.521, CH_2Cl_2). IR: 3072, 2995, 2951, 2929, 2852, 1726, 1512, 1253 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.76 (t, J = 2 Hz, 1H), 7.19-7.23 (m, 2H), 6.83-6.87 (m, 2H), 5.74-5.83 (m, 1H), 4.99-5.04 (m, 2H), 4.50 (A of AB, J = 11 Hz, 1H), 4.44 (B of AB, J = 11 Hz, 1H), 4.13-4.19 (m, 1H), 4.04 (dddd, J = 12, 9, 3, 2 Hz, 1H), 3.95-4.01 (m, 1H), 3.81 (pentet, J = 6 Hz, 1H), 3.78 (s, 3H), 2.61 (dd, J = 6, 2 Hz, 2H), 2.14-2.28 (m, 2H), 1.65-1.76 (m, 2H), 1.55-1.61 (m, 1H), 1.42-1.51 (m, 2H), 1.39 (s, 3H), 1.35 (s, 3H), 1.08-1.16 (m, 1H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.5, 159.3, 135.0, 130.2, 129.5, 117.0, 113.9, 98.4, 71.8, 70.7, 68.4, 65.9, 65.4, 55.3, 49.2, 43.3, 42.6, 41.8, 37.6, 30.2, 25.8, 19.8, 18.1, -4.3, -4.6. Anal. calcd. for $C_{29}H_{48}O_6Si$: C 66.88, H 9.29. Found: C 66.89, H 8.90.

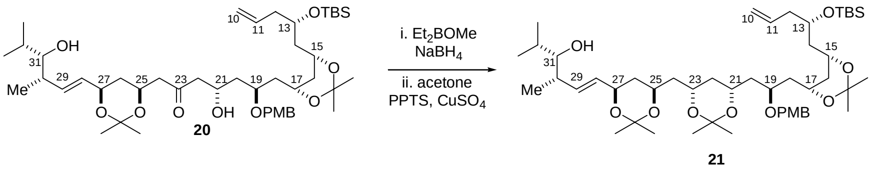
C10-C33 ketone (20):



To a cooled (-10 °C) solution of ketone **2** (336 mg, 1.1 mmol, 1.2 equiv) in ether (12 mL) was added triethylamine (0.39 mL, 2.8 mmol, 3.0 equiv) by syringe. Chlorodicyclohexylborane (2.3 mL, 1.0 M in hexanes, 2.3 mmol, 2.4 equiv) was then added by syringe over 5 min, resulting in the formation of a white precipitate. The resulting mixture was stirred for 30 min at –10 °C then cooled to –78 °C. A solution of aldehyde **3** (488 mg, 0.94 mmol, 1.0 equiv) in ether (2 mL) was then added dropwise by cannula over 20 min. The flask originally containing the aldehyde was rinsed with ether (2 mL), and this solution was also added by cannula. The resulting mixture was stirred for 3 h at –78 °C, then placed in a freezer at -28 C for 21 h. The reaction mixture was then quenched with pH 7 buffer (10 mL), methanol (15 mL), and aqueous hydrogen peroxide (30%, 15 mL). The solution was vigorously stirred and allowed to warm to room temperature. After 3 h the reaction was diluted with brine (10 mL) and CH_2Cl_2 (15 mL), and the phases were separated. The aqueous phase was back-extracted with CH_2Cl_2 (3 x), and the combined organic layers were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. Flash chromatography (3:1 hexanes/ethyl acetate) provided the desired ketone as a clear oil (634.1 mg, 0.78 mmol, 83%, >10:1 dr).

R_f: 0.15 (5:1 hexanes/ethyl acetate). $[\alpha]_D = +=8.92$ (*c* 0.54, CH_2Cl_2). IR: 3495, 2951, 2858, 1710, 1514, 1379, 1250, 1037, 973 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.22-7.26 (m, 2H), 6.84-6.88 (m, 2H), 5.75-5.83 (m, 1H), 5.59-5.65 (m, 1H), 5.43-5.48 (m, 1H), 4.98-5.04 (m, 2H), 4.52 (d, J = 10.8 Hz, 1H), 4.46 (d, J = 10.7 Hz, 1H), 4.30-4.38 (m, 3H), 3.90-4.06 (m, 3H), 3.79-3.84 (m, 1H), 3.78 (s, 3H), 3.38 (d, J = 3.5 Hz, 1H), 3.13 (t, J = 5.8 Hz, 1H), 2.69 (dd, J = 16.0, 7.4 Hz, 1H), 2.54 (d, J = 6.2 Hz, 2H), 2.40 (dd, J = 16.0, 5.3 Hz, 1H), 2.29-2.36 (m, 1H), 2.14-2.27 (m, 2H), 1.64-1.74 (m, 4H), 1.46-1.60 (m, 6H), 1.44 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H), 1.20-1.28 (m 1H), 1.08-1.15 (m, 1H), 1.0 (d, J = 6.7 Hz, 3H), 0.9 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.86 (s, 9H), 0.02 (d, J = 5.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.1, 159.3, 135.3, 135.0. 130.4, 129.5, 117.0, 113.9. 98.9, 98.4, 79.7, 72.7, 72.2, 69.8, 68.4, 65.9, 65.5, 64.7, 55.3, 51.3, 49.6, 43.3, 42.3, 41.8, 40.9, 39.3, 37.6, 36.9, 30.5, 30.3, 30.1, 25.9, 19.8, 19.7, 19.6, 18.1, 17.1, 13.8, -4.3, -4.6. HRMS (ESI) calcd: 841.5249 (for $C_{46}H_{78}O_{10}Si$ + Na), found: 841.5256.

Acetonide (21):

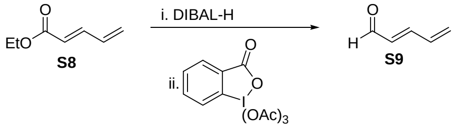


To a cooled (-78 °C) solution of hydroxyketone **20** (622 mg, 0.775 mmol, 1 equiv) in 4:1 THF/methanol (15 mL) was added diethylmethoxyborane (0.930 mL, 0.929 mmol, 1.2 equiv) by syringe. The solution was stirred at –78 °C for 30 min then sodium borohydride (59 mg, 1.55 mmol, 2.0 equiv) was added in a single portion. The ice bath was removed, and after an hour, the reaction was at room temperature, and was quenched with saturated ammonium chloride (4 mL) and ethyl acetate (8 mL). The phases were separated and the aqueous phase was back extracted with ethyl acetate (5 x). The combined organics were dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The resulting pale yellow oil was dissolved in methanol (25 mL) and the solvent was distilled under ambient atmosphere in order to remove chelated boron species. This procedure was conducted four times to provide the crude diol (605.8 mg) as a pale yellow oil which was used in the nxt step without purification.

To a solution of the crude diol in acetone (7.4 mL) was added anhydrous copper (II) sulfate (236 mg, 1.48 mmol, 2 equiv) and pyridinium *p*-toluene sulfonate (19 mg, 0.078 mmol, 0.1 equiv). This suspension was stirred at room temperature for 8 h, then quenched with triethylamine (0.200 mL), filtered through a short plug of silica over celite. The plug was washed with and the organics were combined and concentrated under reduced pressure. Flash chromatography of the crude material (7:1 hexanes : ethyl acetate) provided acetonide **21** as a viscous pale-yellow oil (549.3 mg, 0.638 mmol, 84% over two steps, >10:1 dr).

R_f: 0.09 (5:1 hexanes/ethyl acetate). $[\alpha]_D$ = +8.9 (*c* 0.81, CH_2Cl_2). IR: 3495, 2943, 1612, 1513, 1464, 1380, 1249, 1199, 938, 835 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (m, 2H), 6.82-6.88 (m, 2H), 5.74-5.83 (m, 1H), 5.60 (dd, J = 15.6, 7.3 Hz, 1H), 5.46 (dd, J = 15.8, 6.3 Hz, 1H), 4.98-5.04 (m, 2H), 4.42 (s, 2H), 4.28-4.35 (m, 1H), 3.93-4.12 (m, 5H), 3.74-3.86 (m, 5H), 3.13 (t, J = 5.8 Hz, 1H), 2.13-2.36 (m, 3H), 1.64-1.74 (m, 2H), 1.52-1.58 (m, 4H), 1.32-1.50 (m, 25H), 1.04-1.28 (m, 3H), 1.0 (d, 6.8 Hz, 3H), 0.82-0.92 (m, 15H), 0.12 (d, 5.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 135.0, 134.8, 131.1, 130.9. 129.2, 116.9, 113.8, 98.6, 98.4, 98.3, 79.7, 72.2, 71.1, 70.3, 68.4, 65.9, 65.6, 65.4, 64.8, 64.5, 55.3, 43.4, 43.1, 42.9, 41.8, 39.3, 37.9, 37.7, 37.6, 30.5, 30.4, 30.3, 25.8, 20.0, 19.9, 19.8, 19.6, 18.0, 17.1, 13.8, -4.2, -4.6. HRMS (ESI) calcd: 883.5725 (for $C_{49}H_{84}O_{10}Si$ + Na), found: 883.5731.

Penta-2,4-dienal:

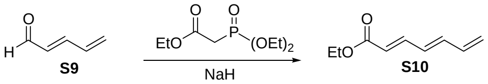


To a cooled (-78 °C) solution of **S8**[8] (4.8 g, 42.8 mmol, 1 equiv) in CH_2Cl_2 (70 mL) was added diisobutylaluminum hydride (90 mL, 1M in hexanes, 90 mmol, 2.1 equiv) slowly, by cannula. The ice bath was removed and the reaction was stirred for 3 h at which point it was at room temperature. The reaction was diluted with ether and quenched by the sequential addition of water (3 mL), 1M sodium hydroxide (6 mL), and additional water (3 mL), resulting in the formation of a white precipitate. This suspension was stirred for 45 min then magnesium sulfate was directly added and the mixture was stirred for an additional 5 min. Filtration through celite and evaporation of solvents under reduced pressure (*ca*. 20 mm Hg) cleanly provided the desired allylic alcohol (3.5 g, 41.6 mmol, 97%). This material was used directly in the next reaction without further purification.

To a cooled (0 °C) solution of the allylic alcohol in CH_2Cl_2 (85 mL) was added Dess-Martin Periodinane (19 g, 45.0 mmol, 1.05 equiv) in one portion. The suspension was slowly warmed to room temperature and stirred for 14 h. The mixture was filtered through a plug of silica over a pad of celite (washed repeatedly with CH_2Cl_2), then quenched with saturated sodium bicarbonate (6 mL). The phases were separated and the organic layer was extracted with sodium bicarbonate (2 x 3 mL) and brine (4 mL). The organic layer was dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. Flash chromatography (CH_2Cl_2) provided the known volatile dienal **S9**[9] as a 15:1 mixture of isomers favoring the desired trans dienal (2.20 g, 26.8 mmol, 63%).

R_f: 0.57 (CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ 9.58 (d, J = 7.9 Hz, 1H), 7.08 (dd, J = 15.4, 10.9 Hz, 1H), 6.58 (dddd, J = 16.9, 11.4, 10, 0.7 Hz, 1H), 6.16 (ddd, J = 15.4, 7.9, 0.5 Hz, 1H), 5.71-5.75 (m, 1H), 5.60-5.63 (m, 1H). ^{13}C NMR (100 MHz): δ 193.8, 151.9, 134.8, 132.4, 127.6.

Hepta-2,4,6-trienoic acid ethyl ester:



To a cooled (0 °C) suspension of sodium hydride (900 mg, 37.5 mmol, 1.4 equiv) in THF (134 mL) was added triethyl phosphonoacetate (8.1 mL, 40.0 mmol, 1.5 equiv) slowly by syringe. Rapid hydrogen gas evolution occurred as the sodium hydride was consumed. After stirring at 0 °C for 30 min., a solution of **S9** (2.20 g, 26.8 mmol, 1 equiv) in THF (10 mL) was added by cannula and the resulting red solution was set to reflux. After 16 h, the reaction was quenched with saturated sodium bicarbonate (10

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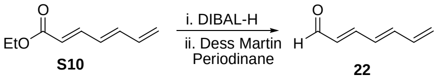
[8] For the synthesis of **S8**, see: J. Rodriguez, B. Waegell, *Synthesis* **1988**, 534-535.

[9] J. J. Tufariello, H. Meckler, K. Senaratne, K. Pushpananda, *Tetrahedron* **1985**, *41*, 3447-3453.

mL). The phases were separated and the aqueous layer was extracted with ether (3 x). The combined organic layers were extracted with brine, dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. Flash chromatography (20:1 hexanes/ethyl acetate) provided the known trienoate **S10**[10] as a clear, colorless oil (2.12 g, 14.0 mmol, 52%).

R_f: 0.65 (5:1 hexanes/ethyl acetate). IR: 2924, 2360, 2342, 1718, 1266, 1182, 1031. ^{1}H NMR (500MHz, $CDCl_3$): δ 7.28 (dd, J = 15.3, 11.2 Hz, 1H), 6.53 (dd, J = 15, 10.8 Hz, 1H), 6.40 (ddd, J = 16.7, 10.4, 10.4 Hz, 1H), 6.30 (dd, J = 15, 11.2 Hz, 1H), 5.88 (d, J = 15.3 Hz, 1H), 5.40 (d, J = 16.7 Hz, 1H), 5.29 (d, J = 10 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 144.1, 140.8, 136.2, 130.4, 121.6, 121.6, 60.3, 14.3. HRMS (ESI) calcd: 153.0910 (for $C_9H_{12}O_2$ + H), found: 153.0906.

Hepta-2,4,6-trienal (22):



To a cooled (-78 °C) solution of **S10** (2.1 g, 14.0 mmol, 1 equiv) in CH_2Cl_2 (35 mL) was added diisobutylaluminum hydride (29 mL, 1M in hexanes, 90 mmol, 2.1 equiv) slowly, by cannula. The ice bath was removed and the reaction was stirred for 4 h at which point it was at room temperature. The reaction was diluted with ether (35 mL), and quenched by the sequential addition of water (1.5 mL), 1M sodium hydroxide (3 mL), and additional water (1.5 mL) resulting in the formation of a white precipitate. This suspension was stirred for 30 min then magnesium sulfate was directly added and the mixture was stirred for an additional 5 min. The solution was filtered through celite and concentrated under reduced pressure to cleanly provide the desired trienol (1.4 g, 13.0 mmol, 92%) as a white solid. A portion of this material was used directly in the next reaction without further purification.

To a cooled (0 °C) solution of the trienol (400 mg, 3.6 mmol, 1 equiv) in CH_2Cl_2 (18 mL) was added Dess-Martin Periodinane (1.6 g, 3.8 mmol, 1.05 equiv) in one portion. The suspension was slowly warmed to room temperature and stirred for 12 h. The mixture was filtered through a plug of silica over a pad of celite (washed repeatedly with CH_2Cl_2), then quenched with saturated sodium bicarbonate. The phases were separated, and the organic layer was washed with sodium bicarbonate (2 x) and brine. The organic layer was dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure. The crude product was purified by flash chromatography (CH_2Cl_2) to provide a 10:1 isomeric mixture of trienal (**22**) as a clear yellow oil (366 mg, 3.4 mmol, 93%).

R_f: 0.50 (CH_2Cl_2). IR: 3021, 2817, 2730, 1681, 1615, 1168, 1114, 1017, 979, 918, 887. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.56 (d, J = 8.0 Hz, 1H), 7.11 (dd, J = 15.3, 11.1 Hz, 1H), 6.65 (dd, J = 15.0, 10.7 Hz, 1H), 6.40-6.50 (m, 2H), 6.16 (dd, J = 15.2, 7.9

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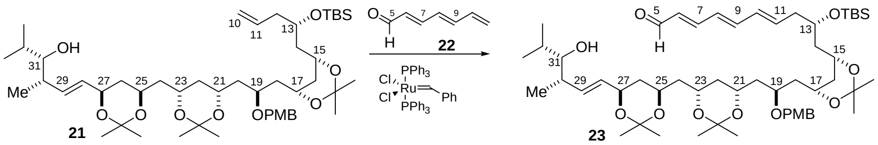
[10] F. Bohlmann, M. Ganzer, M. Krueger, E. Nordhoff, *Tetrahedron* **1983,** *39*, 123-128.

Hz, 1H), 5.48 (d, J = 17.3 Hz, 1H), 5.40 (d, J = 10.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 193.5, 151.5, 142.7, 135.9, 131.8, 130.4, 123.3.

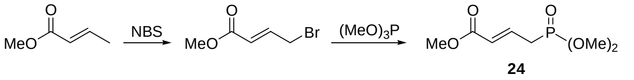
Trienal (23):



To a solution of **21** (143 mg, 0.17 mmol, 1 equiv) and trienal **22** (45 mg, 0.42 mmol, 2.5 equiv) in CH_2Cl_2 (3.3 mL) was added benzylidene-bis(tricyclohexyl phosphine)dichlororuthenium (Grubb's 1st generation catalyst, 7 mg, 0.0083 mmol, 0.05 equiv). The reaction was heated to reflux for 24 h at which time TLC analysis showed only partial conversion to the desired aldehyde. Additional catalyst was added (7 mg) and the reaction was heated to reflux for an additional 24 h at which point TLC analysis revealed a minor amount of starting material remaining. The reaction was deemed complete, and was cooled to room temperature and quenched by the addition of activated charcoal (700 mg, 50 equiv relative to catalyst). After stirring for 4 h, the suspension was filtered through a silica plug over a pad of celite and washed with ethyl acetate, and concentrated under reduced pressure to a pale yellow oil. Flash chromatography (7:1 hexanes/ethyl acetate) provided trienal **23** as a 4:1 mixture of isomers (112.2 mg, 0.119 mmol, 72%).

R_f: 0.21 (5:1 hexanes/ethyl acetate). $[\alpha]_D$ = +8.8 (*c* 1.23, CH_2Cl_2). IR: 3492, 2946, 1679, 1613, 1513, 1380, 1250, 1108, 938, 836 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.53 (d, J = 8.0 Hz, 1H), 7.22-7.24 (m, 2H), 7.04-7.12 (dd, J = 15.1, 11.2 Hz, 1H), 6.84-6.87 (m, 2H), 6.62 (dd, J = 14.7, 10.7 Hz, 1H), 6.33 (dd, J = 14.8, 11.2 Hz, 1H), 6.18 (dd, J = 15.2, 10.8 Hz, 1H), 6.12 (dd, J = 8.1, 15.4 Hz, 1H), 5.98-6.04 (m, 1H), 5.45-5.63 (m, 2H), 4.41-4.47 (m, 2H), 4.29-4.35 (m, 1H), 3.93-4.12 (m, 6H), 3.80-3.90 (m, 2H), 3.79 (s, 3H), 3.13 (t, J = 5.8 Hz, 1H), 2.24-2.46 (m, 3H), 1.66-1.74 (m, 2H), 1.52-1.58 (m, 4H), 1.35-1.49 (m, 22H), 1.20-1.28 (m, 2H), 1.06-1.15 (m, 2H), 1.0 (d, J = 6.8 Hz, 3H), 0.86-0.91 (m, 16H), 0.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 159.2, 152.3, 142.9, 138.4, 134.8, 132.0, 131.1, 130.9, 129.4, 128.3, 113.9, 98.6, 98.5, 98.4, 79.7, 72.2, 71.1, 70.6, 68.3, 65.8, 65.6, 65.4, 64.8, 64.5, 55.3, 43.6, 43.1, 42.9, 40.9, 39.3, 37.9, 37.7, 30.5, 30.4, 30.3, 25.8, 20.0, 19.9, 19.6, 18.0, 17.1, 13.8, -4.3, -4.6. HRMS (ESI) calcd: 963.5988 (for $C_{54}H_{88}O_{11}Si$ + Na), found: 963.5978.

Trimethyl-4-phosphonocrotonate (24):



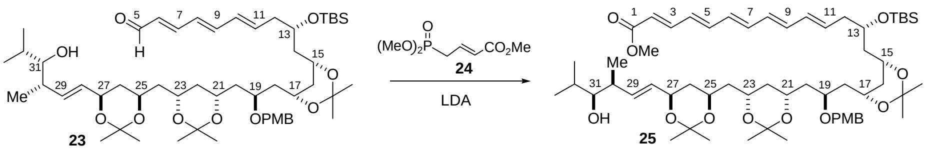
To a refluxing solution of methyl crotonate (5.0 g, 50 mmol, 1 equiv) and *N*-bromosuccinimide (9.8 g, 55 mmol, 1.1 equiv) in chlorobenzene (50 mL) was added benzoyl peroxide (242 mg, 0.02 equiv) in three equal portions. After refluxing for 2 h, the mixture was cooled to 0 °C and allowed to stand overnight (0 °C). The resulting suspension was filtered cold through celite and concentrated under reduced pressure. Flash chromatography (6:1 hexanes/ethyl acetate) provided methyl γ-bromocrotonate as a clear, colorless oil (5.53 g, 31 mmol, 62%) with spectral properties identical to those reported in the literature.[11]

R_f: 0.45 (5:1 hexanes/ethyl acetate). IR: 2952, 1723, 1658, 1436, 1323, 1136, 976 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98-7.02 (m, 1H), 6.0 (dt, J = 15.4, 1.2 Hz, 1H), 4.0 (dd, J = 7.4, 1.2 Hz, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 141.9, 124.2, 51.9, 29.1.

To a solution of methyl γ-bromocrotonate (1.0 g, 5.6 mmol, 1 equiv) in toluene (11 mL) was added trimethyl phosphite (1.3 mL, 11.2 mmol, 2 equiv) and the reaction was heated to reflux for 20 h then cooled to room temperature and concentrated under reduced pressure. Flash chromatography (ethyl acetate) provided trimethyl-4-phosphonocrotonate (898 mg, 4.2 mmol, 77%) as a clear, colorless oil.

R_f: 0.15 (ethyl acetate). IR: 3472, 2956, 2853, 1723, 1657, 1439, 1262, 1031, 886 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.85 (ddd, J = 15.4, 7.8, 7.8 Hz, 1H), 5.92-5.98 (m, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 2.74 (ddd, J = 23.07, 7.9, 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 137.4, 137.2, 125.7, 125.5, 52.9, 52.8, 51.7, 30.3, 28.9. HRMS (ESI) calcd: 209.0573 (for $C_7H_{13}O_5P$ + H), found: 209.0576.

Pentaenoate (25):



To a cooled (-78 °C) solution of diisopropylamine (0.054 mL, 0.384 mmol, 2.6 equiv) in THF (3 mL) was added *n*-butyllithium (0.204 mL, 0.367 mmol, 2.5 equiv) by syringe. The resulting pale yellow solution was stirred at –78 °C for 10 min. then warmed to room temperature over a period of 25 min. The solution was recooled to –78 °C and a solution of trimethyl-4-phosphonocrotonate (76 mg, 0.367 mmol, 2.5 equiv) in THF (2 mL) was added by cannula. After stirring for 35 min. at –78 °C a solution of trienal **23** (138 mg, 0.147 mmol, 1 equiv) was added by cannula. This mixture was stirred at –78 °C for 30 min. and then warmed to room temperature and stirred for 20 h. The reaction was quenched by the addition of saturated sodium bicarbonate (4 mL) and water (1 mL). The phases were separated and the aqueous layer was back extracted with ethyl acetate (5 x). The combined organic layers were dried over magnesium sulfate, filtered through a silica plug over a pad of celite which was washed with ethyl acetate, and concentrated under reduced pressure. Flash chromatography (3:1 hexanes/ethyl acetate) provided the desired pentaenoate **25** (123.7 mg, 0.121 mmol, 82%) as a bright yellow, viscous oil as an 8:1 mixture of alkene isomers.

R_f: 0.26 (3:1 hexanes/ethyl acetate). $[\alpha]_D$ = +7.3 (*c* 0.47, CH_2Cl_2). IR: 3495, 2991, 2948, 1715, 1616, 1513, 1380, 1250, 1167, 1007, 835 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, J = 14.7, 11.3 Hz, 1H), 7.20-7.24 (m, 2H), 6.84-6.87 (m, 2H), 6.57 (dd, J = 14.7, 11.4 Hz, 1H), 6.24-6.32 (m, 2H), 6.16 (dd, J = 14.8, 10.9 Hz, 1H), 6.09 (dd, J = 15.1, 10.8 Hz, 1H), 5.84 (d, J = 15.3 Hz, 1H), 5.74-5.80 (m, 1H), 5.44-5.62 (m, 2H), 4.41-4.47 (m, 1H), 4.29-4.34 (m, 1H), 3.94-4.12 (m, 5H), 3.80-3.86 (m, 2H), 3.77 (s,

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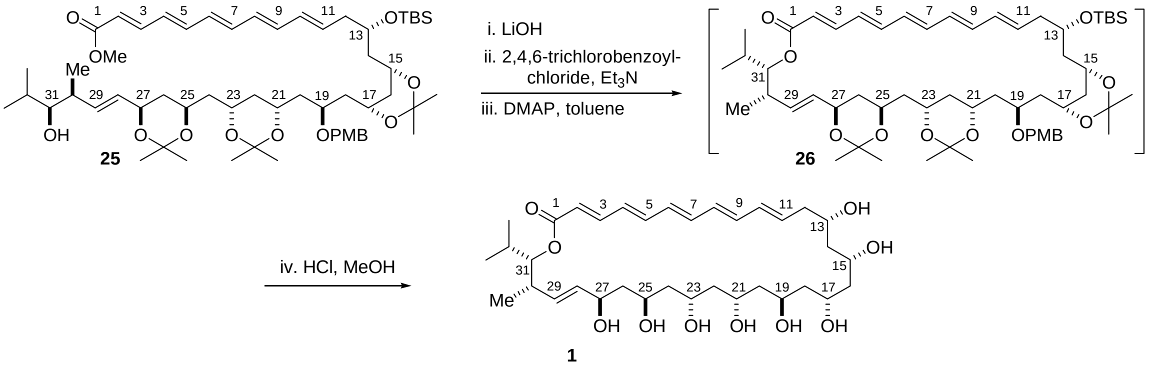
[11] D. K. Bates, X. Li, P. V. Jog, *J. Org. Chem.* **2004**, *69*, 2750 - 2754.

3H), 3.72 (s, 3H), 3.10-3.14 (m, 1H), 2.18-2.40 (m, 3H), 1.64-1.74 (m, 2H), 1.50-1.58 (m, 4H), 1.32-1.48 (m, 25H), 1.20-1.28 (m, 2H), 1.06-1.16 (m, 2H), 1.0 (d, J = 6.7 Hz, 3H), 0.84-0.91 (m, 16H), 0.01 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 159.1, 144.7, 140.9, 137.5, 135.7, 134.8, 133.3, 132.8, 131.2, 131.0, 130.9, 130.6, 129.4, 129.2, 119.7, 113.8, 98.6, 98.4, 98.3, 79.7, 77.3, 72.2, 71.1, 70.3, 68.5, 65.9, 65.6, 65.4, 64.8, 64.5, 55.3, 51.5, 43.6, 43.1, 42.9, 40.9, 39.2, 37.9, 37.7, 37.6, 30.5, 30.4, 30.3, 25.8, 20.0, 19.7, 19.6, 18.0, 17.1, 13.8, -4.3, -4.6. HRMS (ESI) calcd: 1045.6406 (for $C_{59}H_{94}O_{12}Si$ + Na), found: 1045.6404.

RK-397 (1):



The following reactions were conducted in the dark using glassware wrapped in aluminum foil.

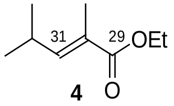
To a stirring solution of pentaenoate **25** (38.3 mg, 0.0374 mmol, 1 equiv) in 4:1:1 THF/methanol/water (5.5 mL) was added 1M lithium hydroxide (1.9 mL, 1.87 mmol, 50 equiv). The yellow, cloudy solution was stirred for 22 h, then diluted with water (2 mL) and ethyl acetate (4 mL). The phases were separated and the aqueous layer was back extracted with ethyl acetate (4 x). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through celite, and concentrated under reduced pressure to give the crude pentenoic acid (37.0 mg, 0.0367 mmol, 97%) which was used directly in the next reaction.

To a solution of the pentenoic acid prepared as described above and triethylamine (0.051 mL, 0.367 mmol, 10 equiv) in THF (3.7 mL) was added 2,4,6-trichlorobenzoyl chloride (0.029 mL, 0.183 mmol, 5 equiv) by syringe. The solution was stirred for 3 h, then filtered through celite and washed with dry THF and concentrated under reduced pressure to provide the mixed anhydride. This material was used directly in the next reaction without further purification.

To a vigorously stirring solution of dimethylaminopyridine (90 mg, 0.733 mmol, 20 equiv) in toluene (27 mL) was added a solution of the crude mixed anhydride prepared as described above in toluene (10 mL) by syringe pump over 14 h. The syringe was rinsed with toluene (2 mL) and this solution was added to the reaction over a period of 30 min. The cloudy mixture was stirred for an additional 5 h, then toluene was removed under reduced pressure. The cloudy oil was diluted in 1:1 hexanes/ethyl acetate (10 mL), filtered through a silica plug over a pad of celite and washed with 1:1 hexanes/ethyl acetate, then concentrated under reduced pressure to afford a bright yellow oil (36.0 mg). A portion of this material was used directly in the next reaction.

To a yellow solution of crude protected RK-397 **26** (19.8 mg, 0.0199 mmol, 1 equiv) in methanol (5 mL) was added 12M hydrochloric acid (0.165 mL, 1.99 mmol, 100 equiv) by syringe. The reaction was stirred at room temperature for 24 h, then quenched with polymer bound piperidine (polystyrene cross-linked with 1% divinylbenzne, 3 to 4 mmol /g piperdine loading, 520 mg, *ca*. 200 - 260 equiv). The suspension was filtered through celite and washed with ethyl acetate and methanol, then concentrated under reduced pressure. Flash chromatography (4:1 chloroform/methanol) provided RK-397 as a mixture of alkene isomers (8.9 mg, .0140 mmol, 70% from **25** based on carrying 54% of compound **26** forward). This material was further purified by reversed phase analytical HPLC (Microsorb C-18, 220 x 5 mm, 2:1 methanol/water, flow rate: 600 μL /min., retention time: 46 min., UV detector: 360 nm). The HPLC purification was repeated to give a pure sample of RK-397 (3.5 mg, 0.0055 mmol) as a pale yellow solid.

R_f: 0.18 (4:1 chloroform/methanol). $[\alpha]_D$ = -26 (*c* 0.30, CH_3OH). IR: 3355, 2936, 2360, 1708, 1691, 1620, 1575, 1325, 1126, 1077, 1012 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 7.31 (dd, J = 15.0, 11.4 Hz, 1H), 6.70 (dd, J = 14.7, 11.2 Hz, 1H), 6.52 (dd, J = 14.7, 10.9 Hz, 1H), 6.44 (dd, J = 14.6, 11.4 Hz, 1H), 6.41 (dd, J = 15.2, 10.6 Hz, 1H), 6.37 (dd, J = 15.4, 11.3 Hz, 1H), 6.29 (dd, J = 14.7, 11.0 Hz, 1H), 6.23 (dd, J = 14.8, 10.5 Hz, 1H), 5.90 (d, J = 15.1 Hz, 1H), 5.86 (ddd, J = 15.4, 10.2, 5.6 Hz, 1H), 5.65 (ddd, J = 16, 4.2, 1.0 Hz, 1H), 5.53 (ddd, J = 15.8, 4.6, 1.2 Hz, 1H), 4.78 (dd, J = 10.0, 2.5 Hz, 1H), 4.19-4.24 (m, 1H), 4.01-4.10 (m, 2H), 3.86-3.99 (m, 4H), 3.79-3.85 (m, 1H), 2.60-2.68 (m, 2H), 2.24 (ddd, J = 13.6, 9.9, 9.9 Hz, 1H), 1.89-1.96 (m, 1H), 1.70 (ddd, J = 13.4, 8.4, 5.0 Hz, 1H), 1.62-1.66 (m, 2H), 1.24-1.56 (m, 11H), 1.19 (ddd, J = 13.7, 10.1, 2.4 Hz, 1H), 1.07 (d, J = 6.9 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CD_3O\Delta$): δ 169.07, 146.87, 142.86, 139.34, 137.17, 134.27, 133.76, 133.52, 132.89, 132.65, 131.14, 121.42, 81.88, 71.45, 69.22, 68.85, 68.45, 67.61, 67.34, 66.25, 64.95, 48.12,47.49, 47.14, 46.86, 46.37, 46.32, 45.32, 44.11, 37.44, 30.70, 20.27, 19.11, 11.34. HRMS (ESI) calcd: 659.3765 (for $C_{35}H_{56}O_{10}$ + Na), found: 659.3779.



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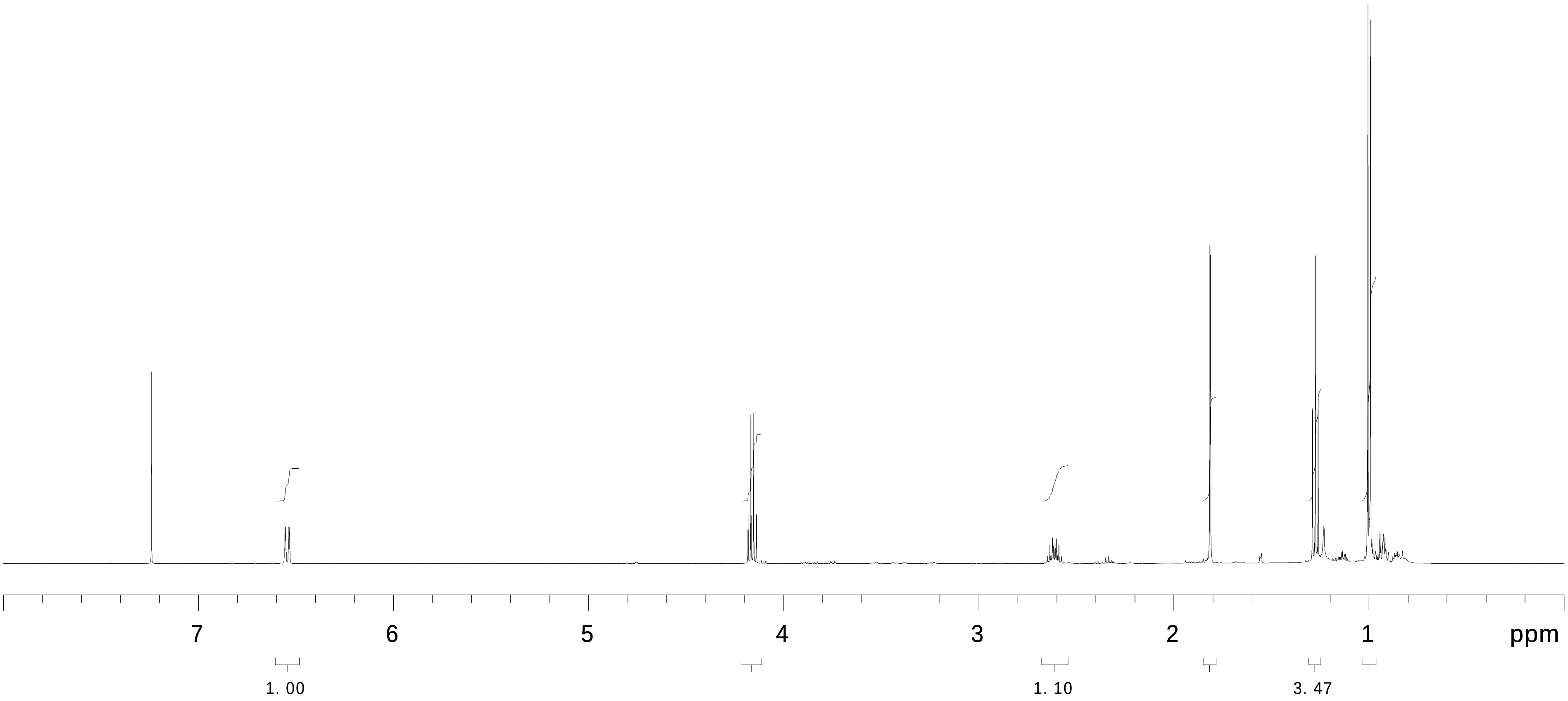

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32 repetitions

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Total time 2 minutes

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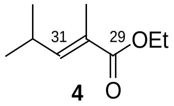
Ambient temperature
File: ajc10-094-3



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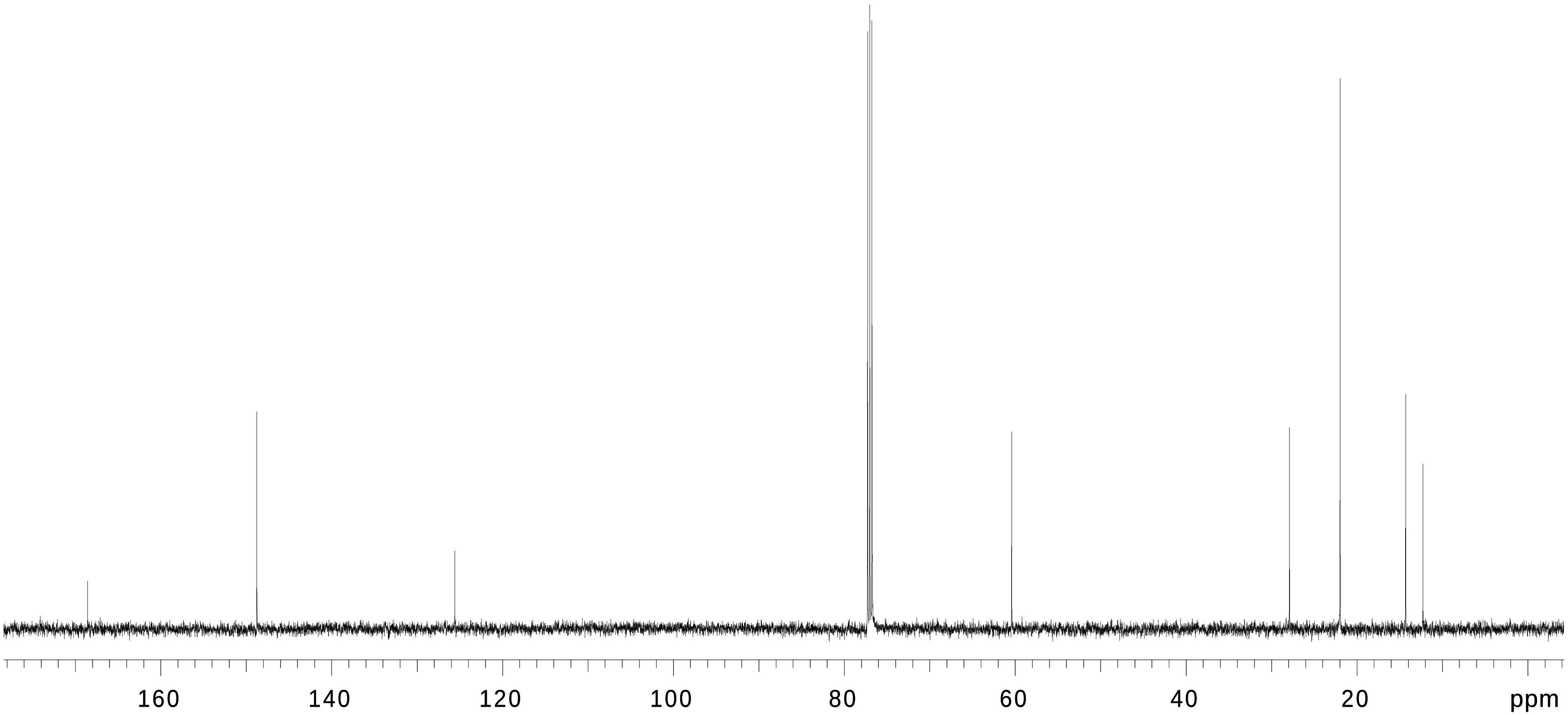

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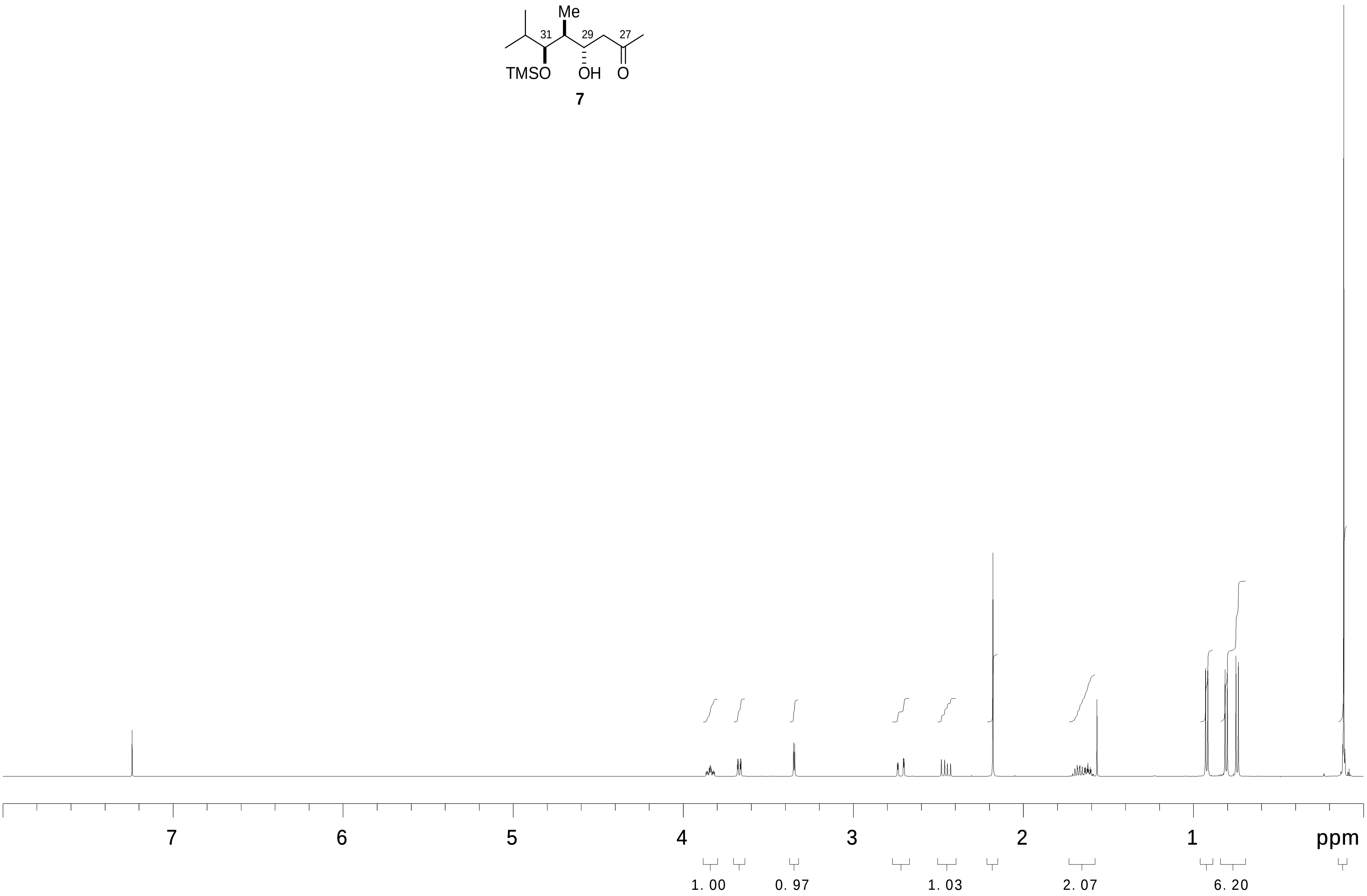
DECOUPLE H1, 500.3697761
Power 44 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 65536
Total time 9 minutes

Solvent: CDCl3
Ambient temperature
File: mjm4-135-2athesis

University of Colorado at Boulder NMR



7

Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
16 repetitions

OBSERVE H1, 500.3674488

DATA PROCESSING
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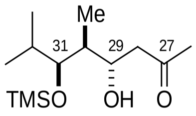
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-105-5

University of Colorado at Boulder NMR



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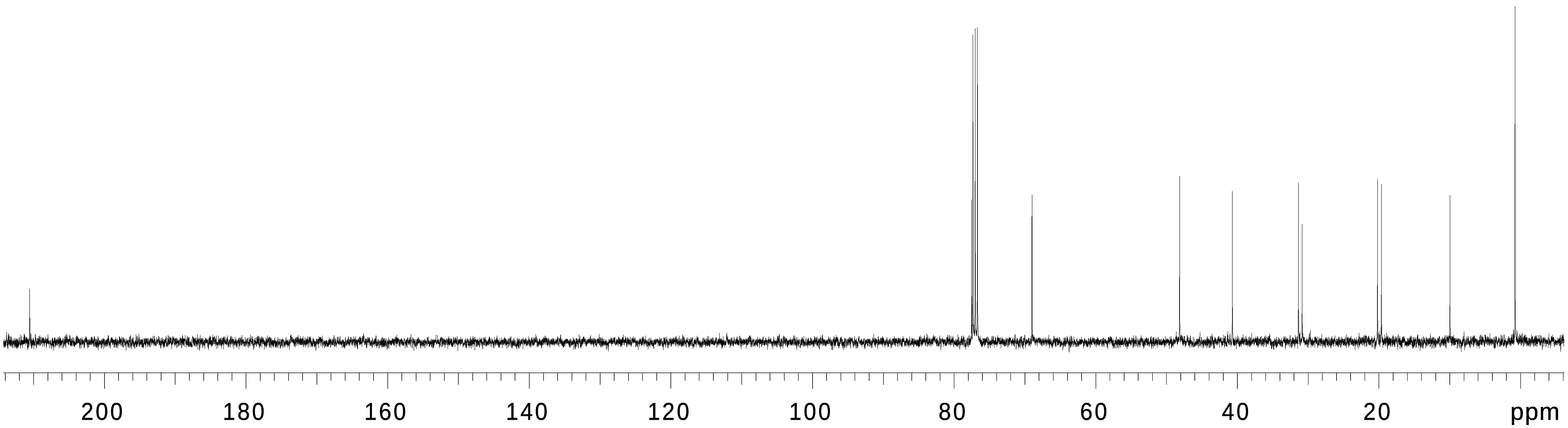

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DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
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Solvent: CDCl3
Ambient temperature
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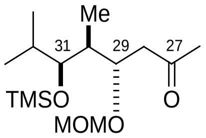

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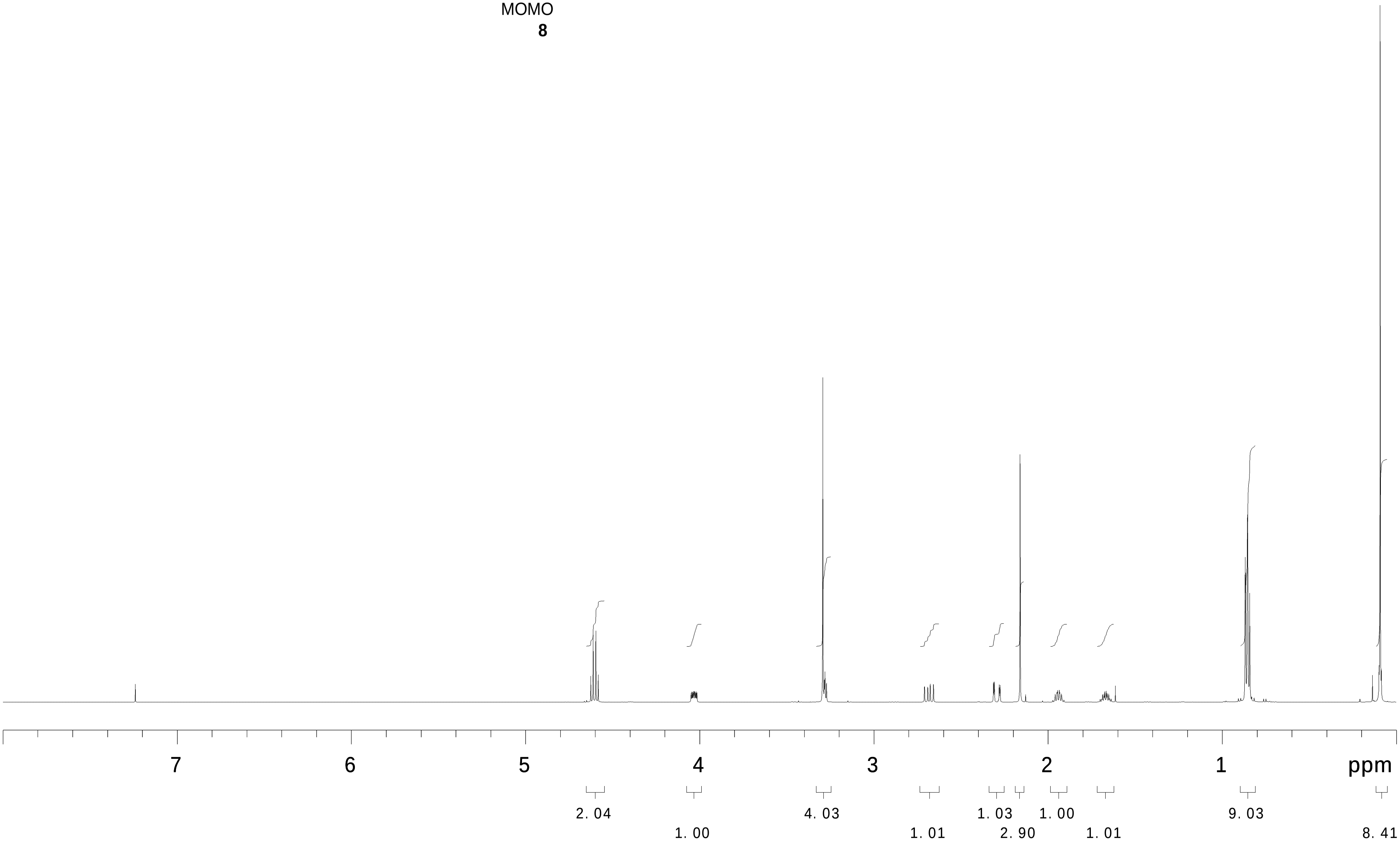

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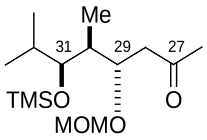
Acq. time 3.000 sec
Width 6505.1 Hz
64 repetitions

OBSERVE H1, 500.3674489

DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-109-3

University of Colorado at Boulder NMR



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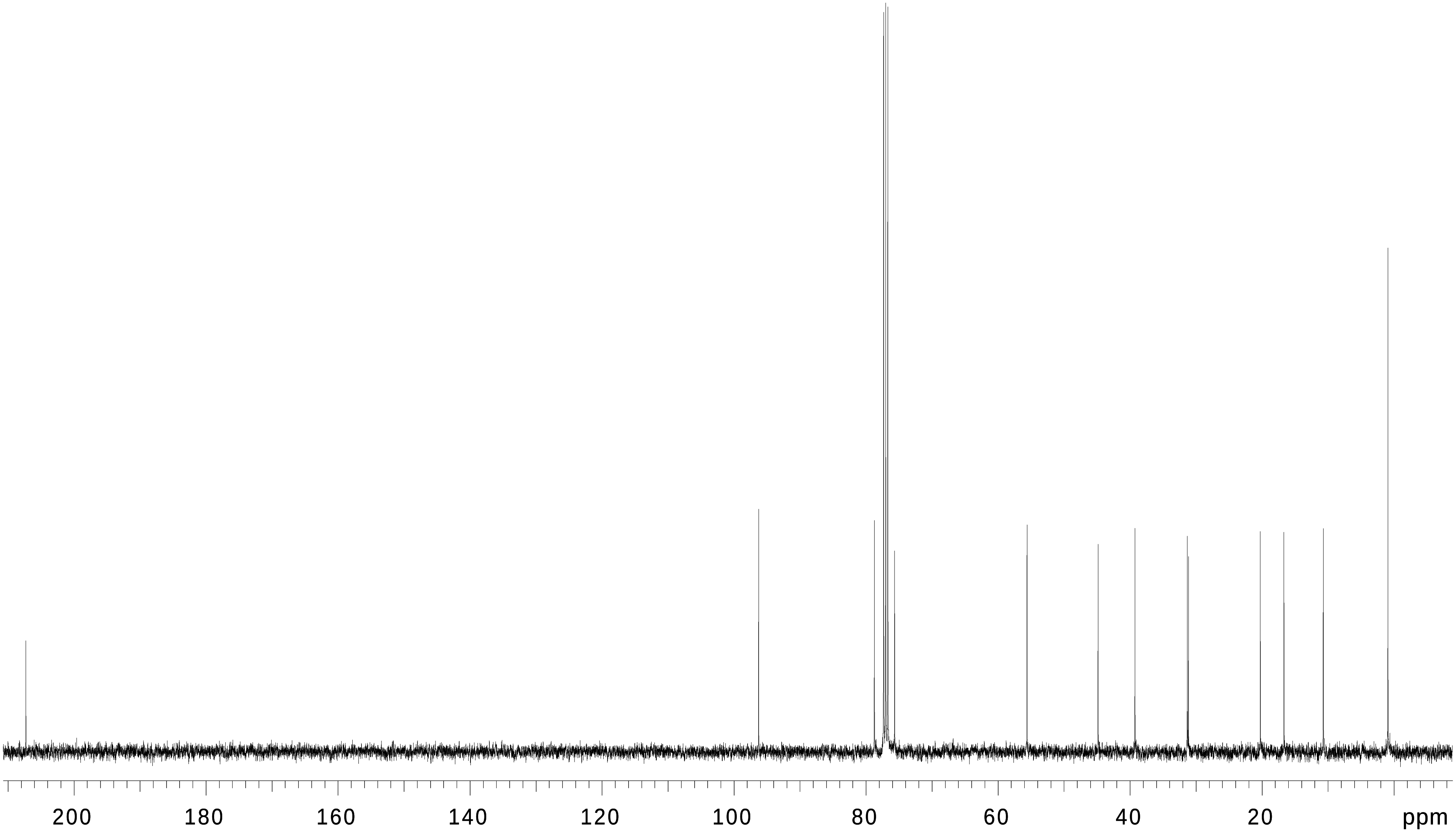

Relax. delay 1.500 sec
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Width 25000.0 Hz
656 repetitions

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DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
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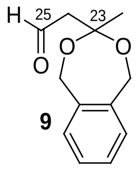
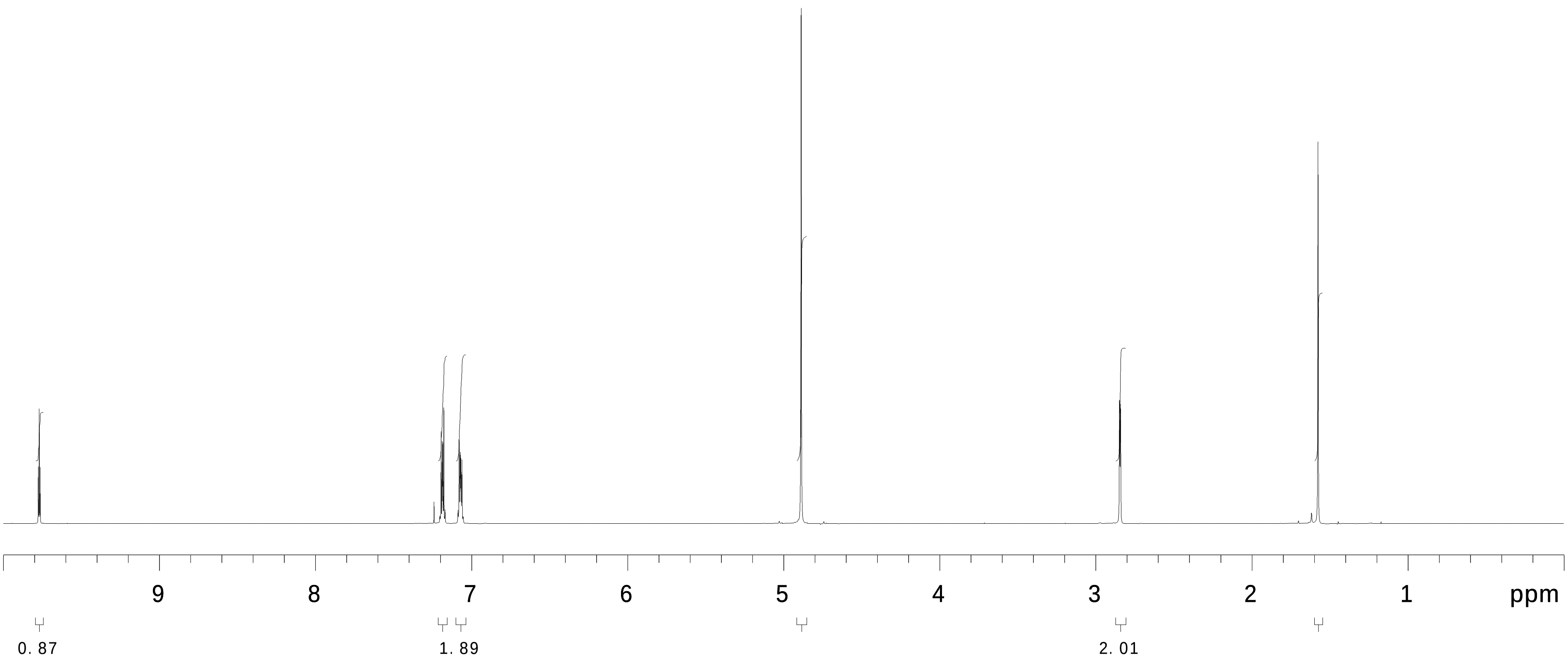
FT size 131072
Total time 30 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-109-3b

University of Colorado at Boulder NMR



9



Relax. delay 0.100 sec
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16 repetitions

OBSERVE H1, 500.3674488

DATA PROCESSING
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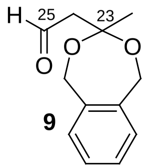
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-114-3

University of Colorado at Boulder NMR



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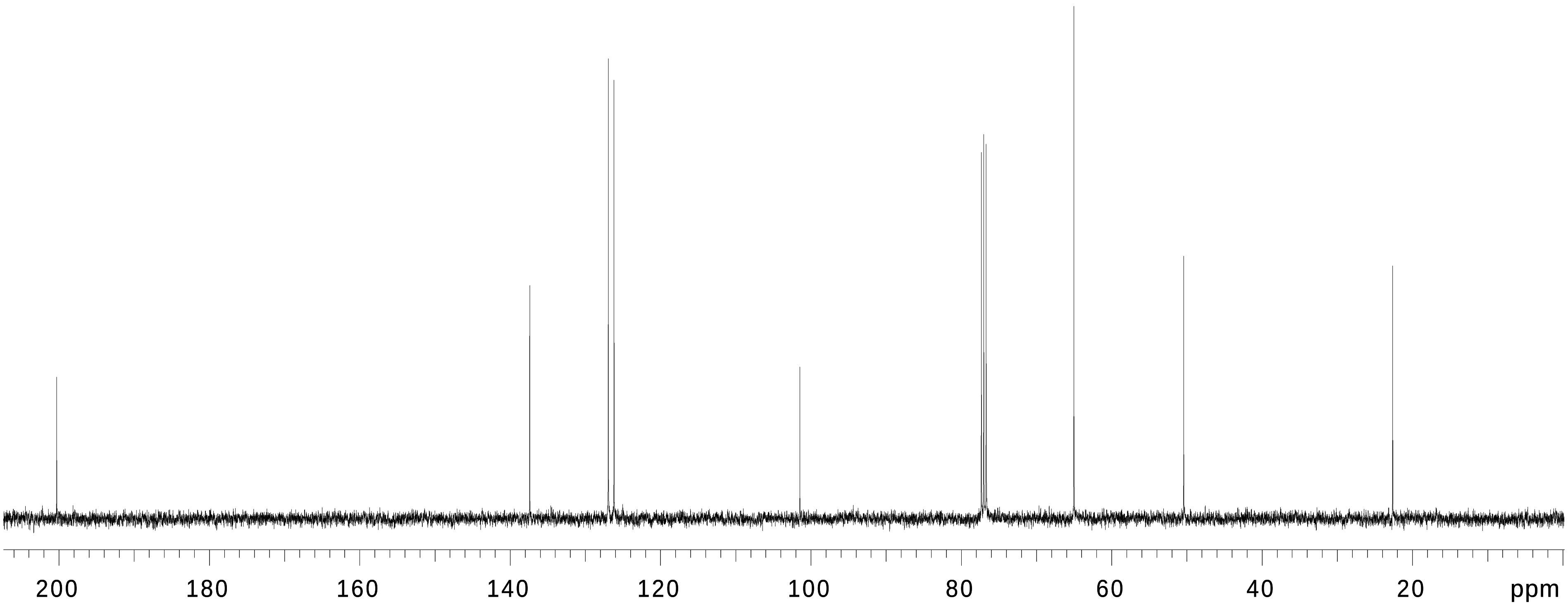

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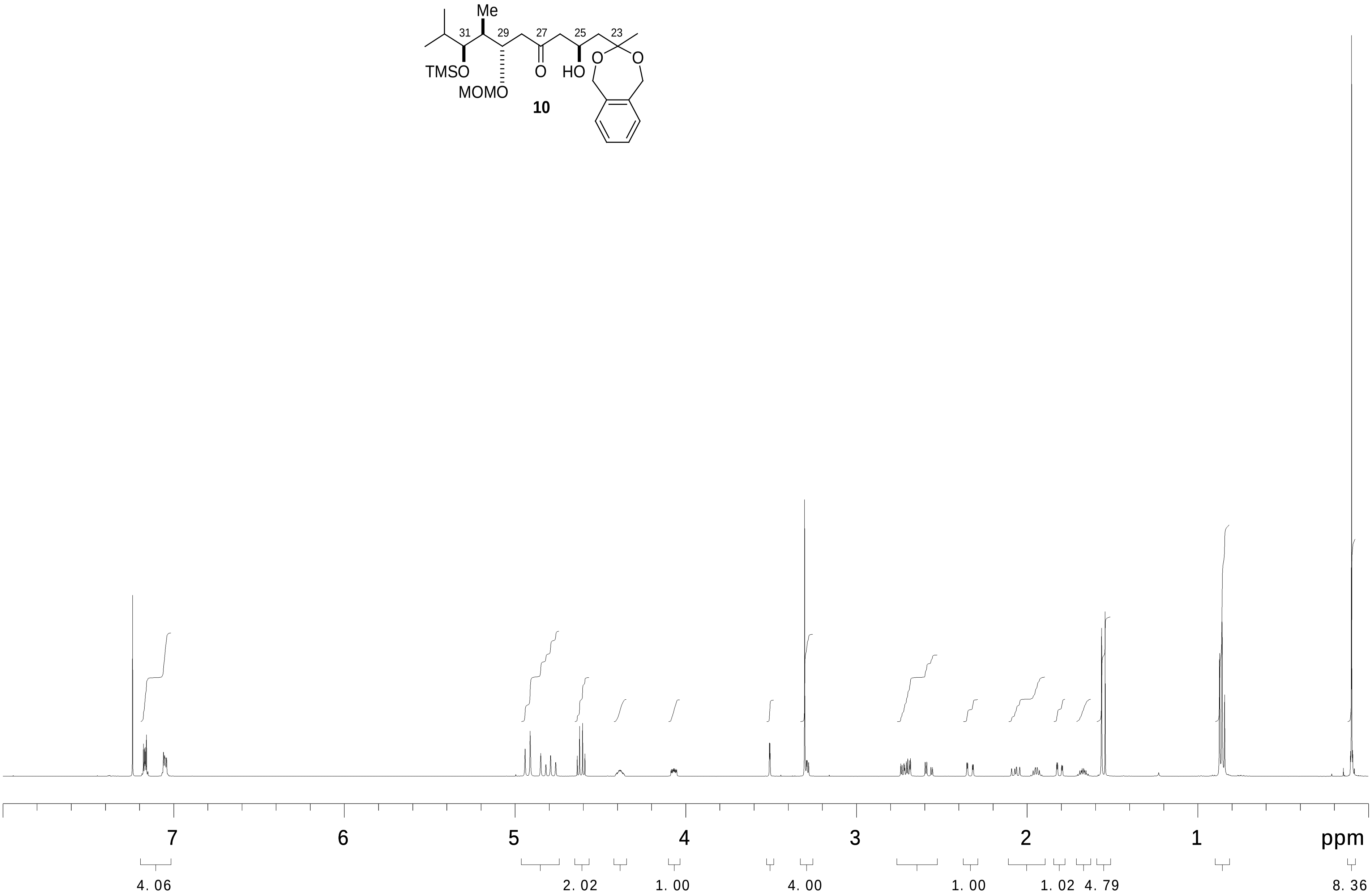
Width 25000.0 Hz
160 repetitions

OBSERVE C13, 100.6189891
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 7 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-114-3b

University of Colorado at Boulder NMR



10

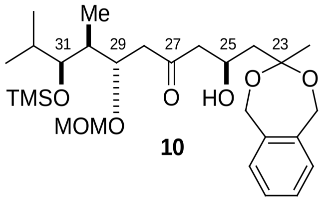
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
36 repetitions

OBSERVE H1, 500.3674488

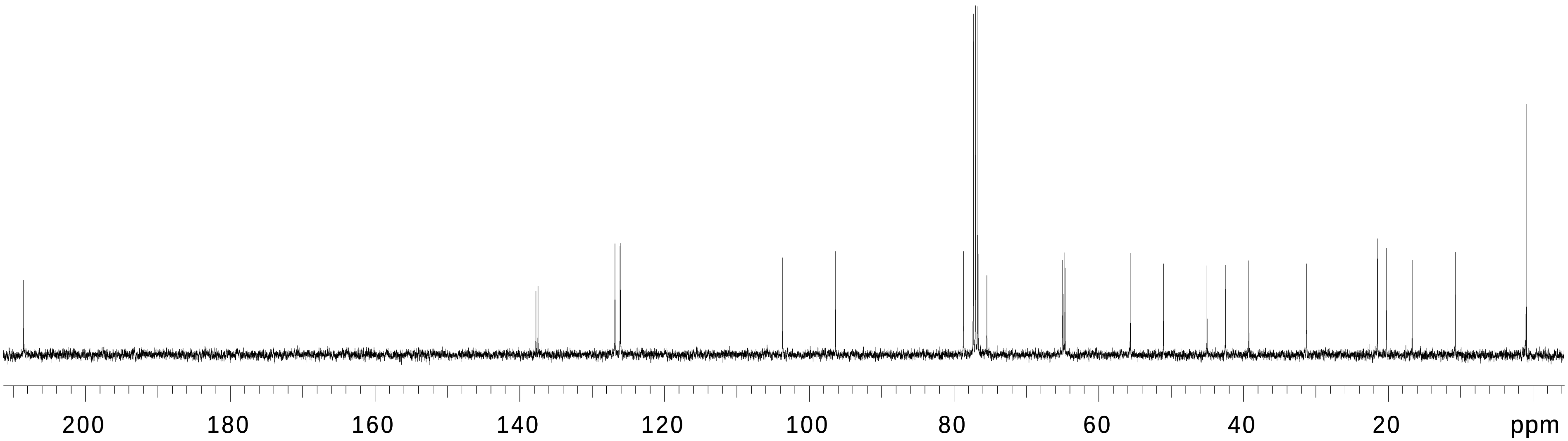
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-117-9

University of Colorado at Boulder NMR



10

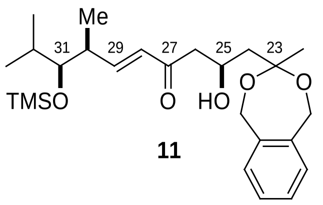


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
352 repetitions

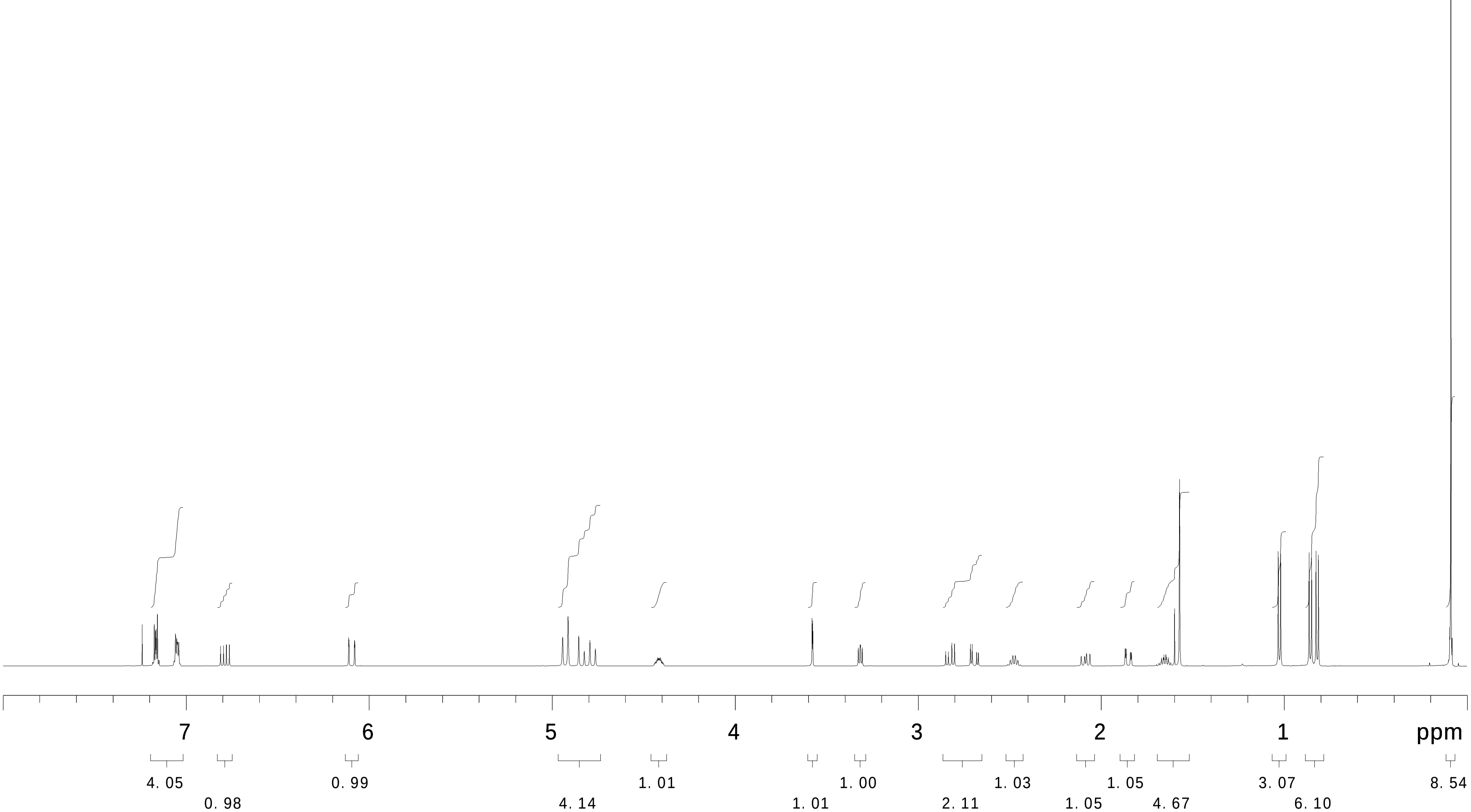
OBSERVE C13, 100.6189880
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 16 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-117-3b



11



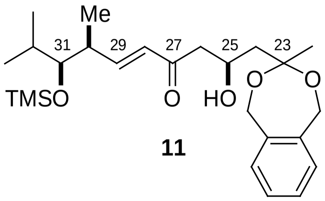
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
17 repetitions

OBSERVE H1, 500.3674489

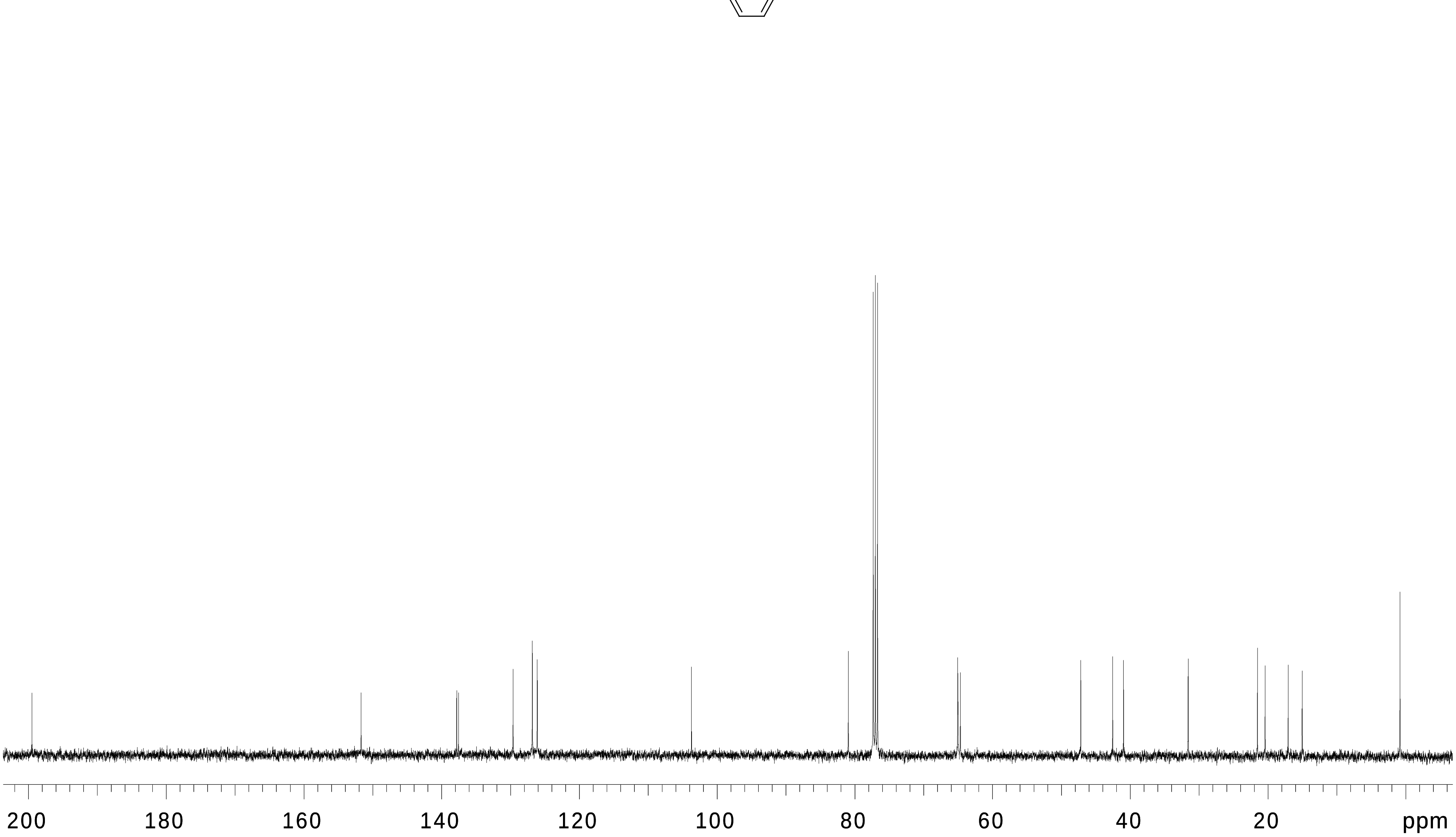
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-121-3

University of Colorado at Boulder NMR



11

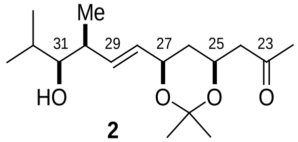


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
832 repetitions

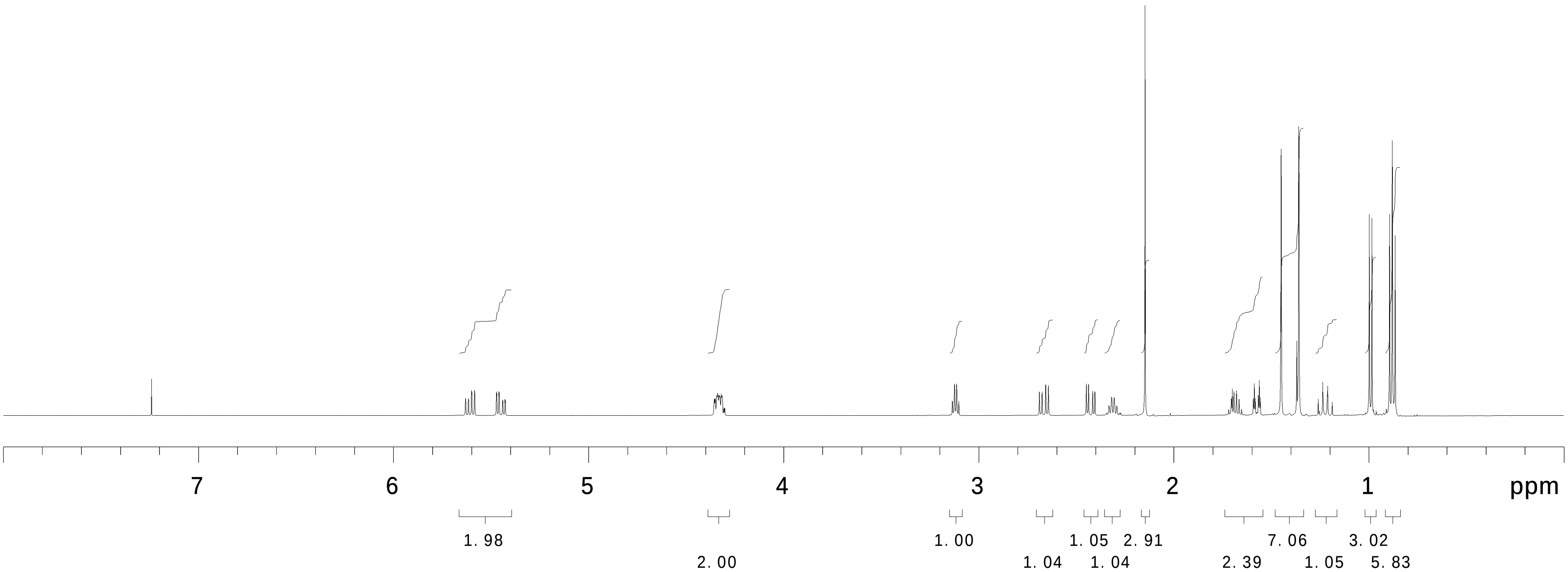
OBSERVE C13, 100.6189872
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 39 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-121-3b



2



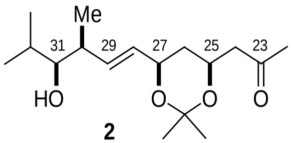
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
7 repetitions

OBSERVE H1, 500.3674488

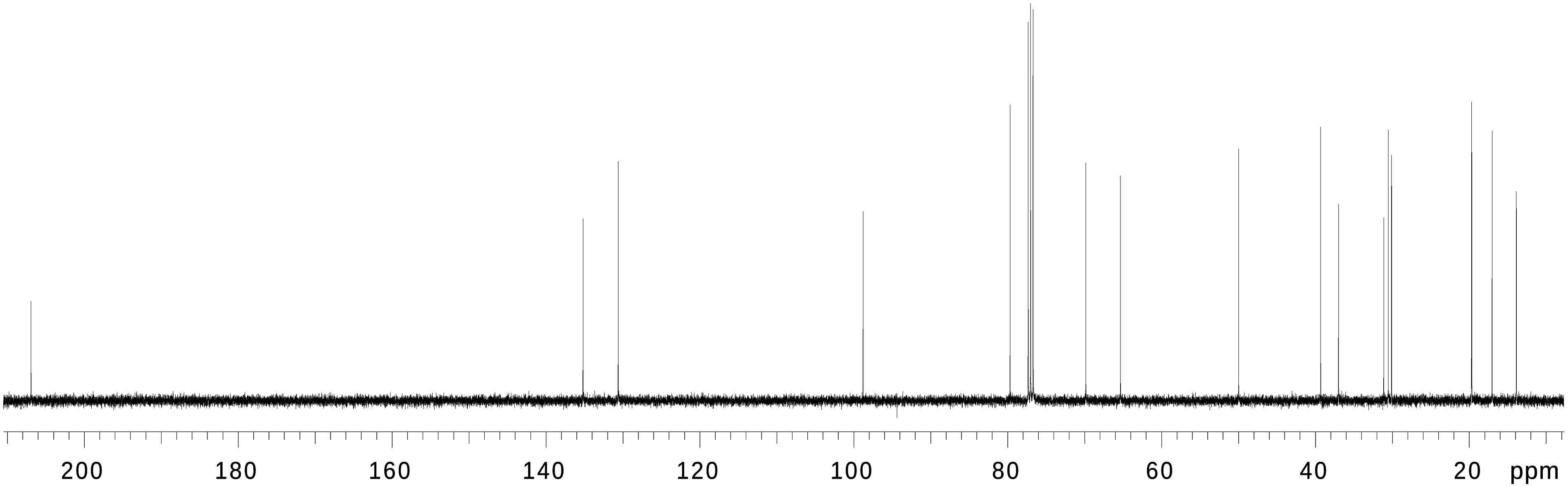
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-127-2

University of Colorado at Boulder NMR



2



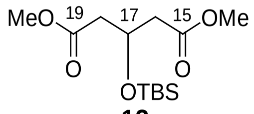
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
1024 repetitions

OBSERVE C13, 100.6189880
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

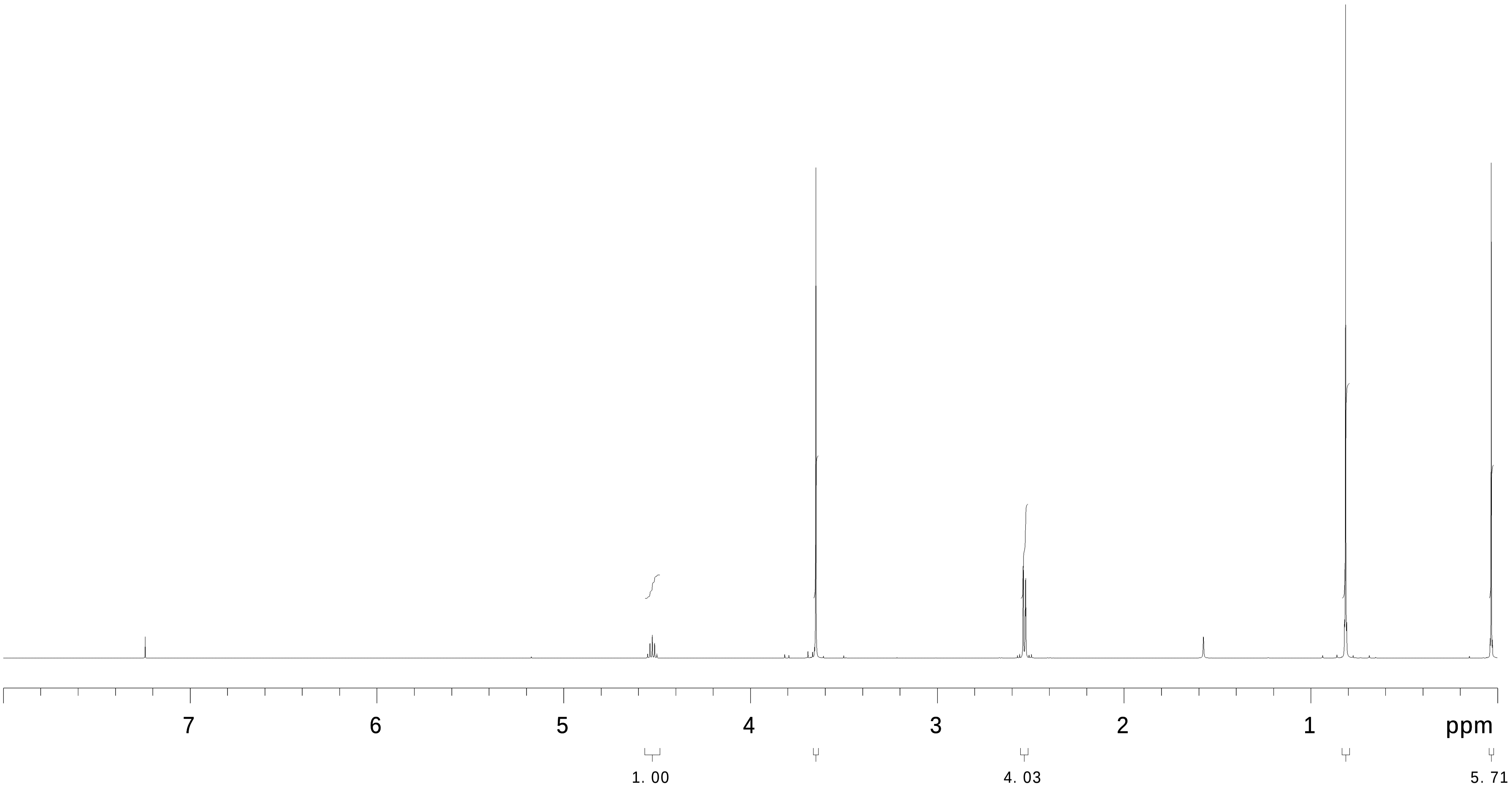
DATA PROCESSING
Line broadening 0.2 Hz
FT size 131072
Total time 48 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-127-2b

University of Colorado at Boulder NMR



12



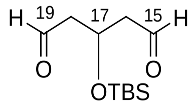
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
16 repetitions

OBSERVE H1, 500.3674490

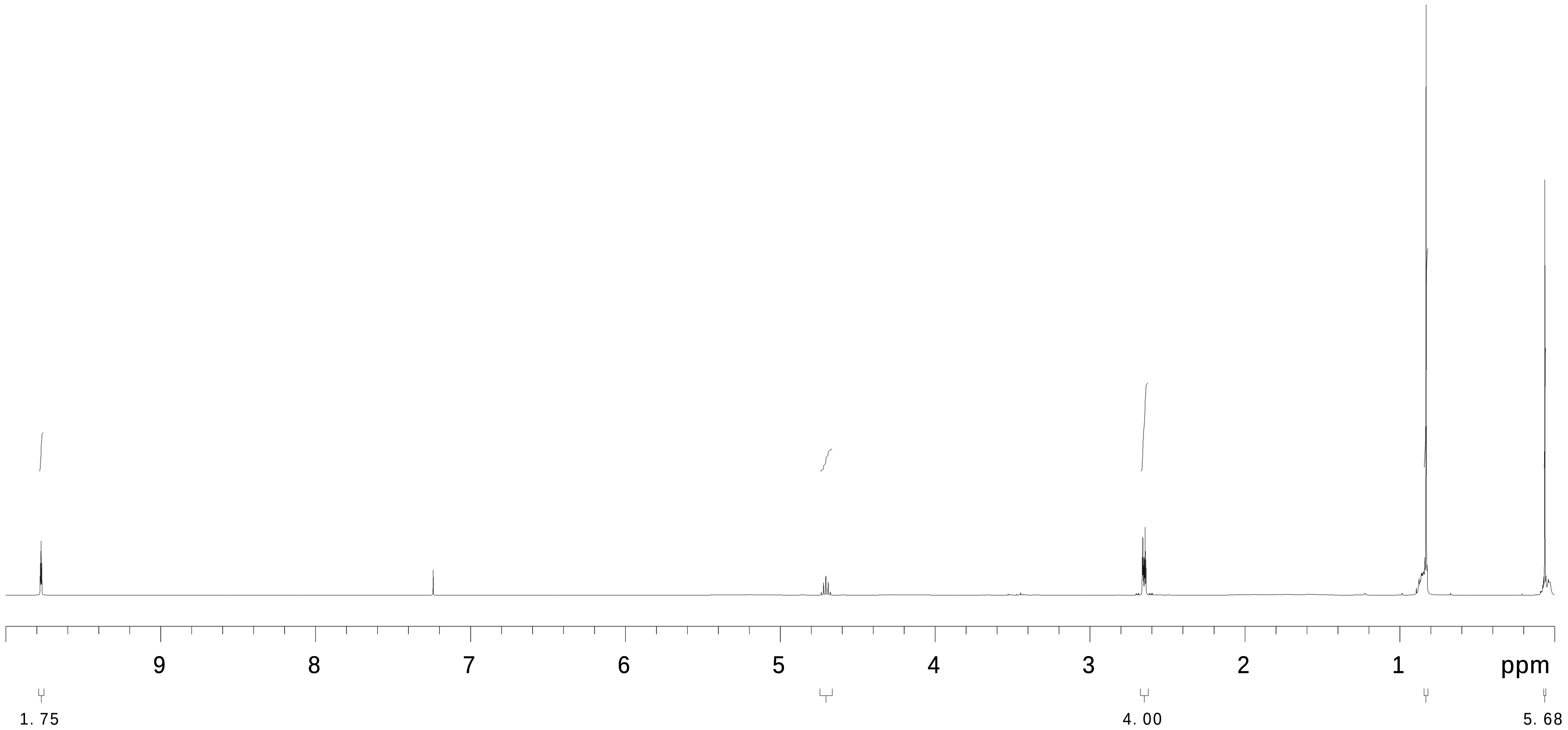
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-74-1

University of Colorado at Boulder NMR



13



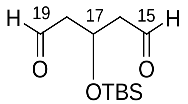
Relax. delay 0.500 sec
Pulse 33.0 degrees
Acq. time 3.000 sec
Width 6000.6 Hz
9 repetitions

OBSERVE H1, 400.1547358

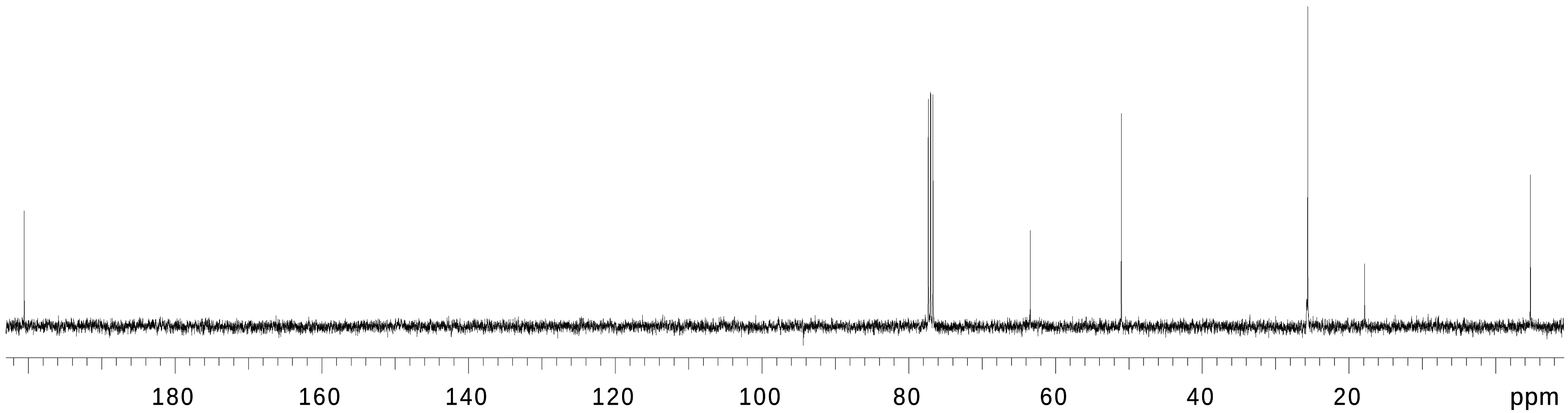
DATA PROCESSING
Line broadening 0.2 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-74-5

University of Colorado at Boulder NMR



13



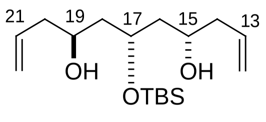
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
128 repetitions

OBSERVE C13, 100.6189868
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

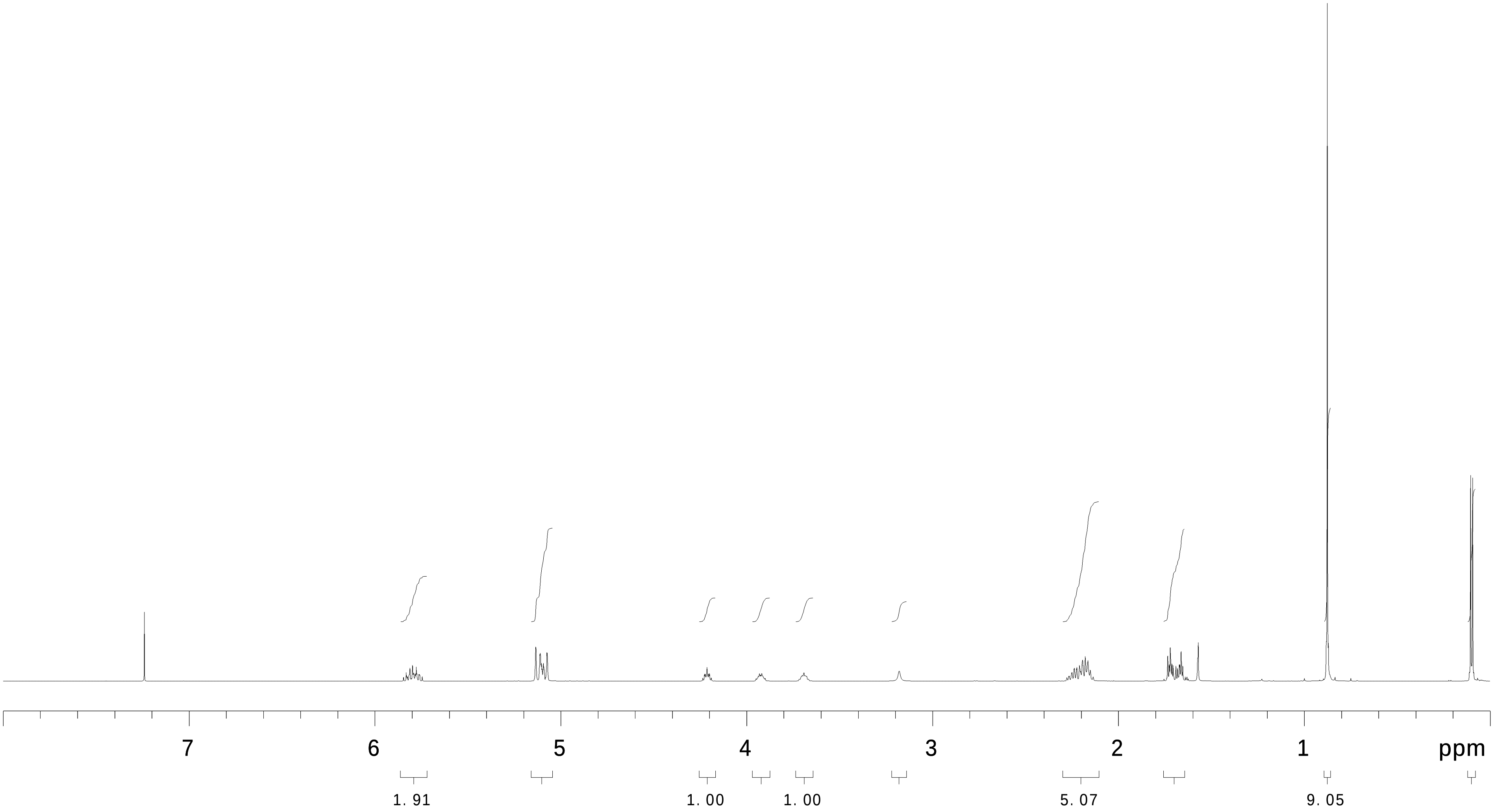
DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 6 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-74-5a

University of Colorado at Boulder NMR



15

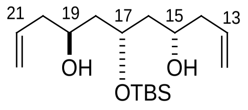


Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
64 repetitions

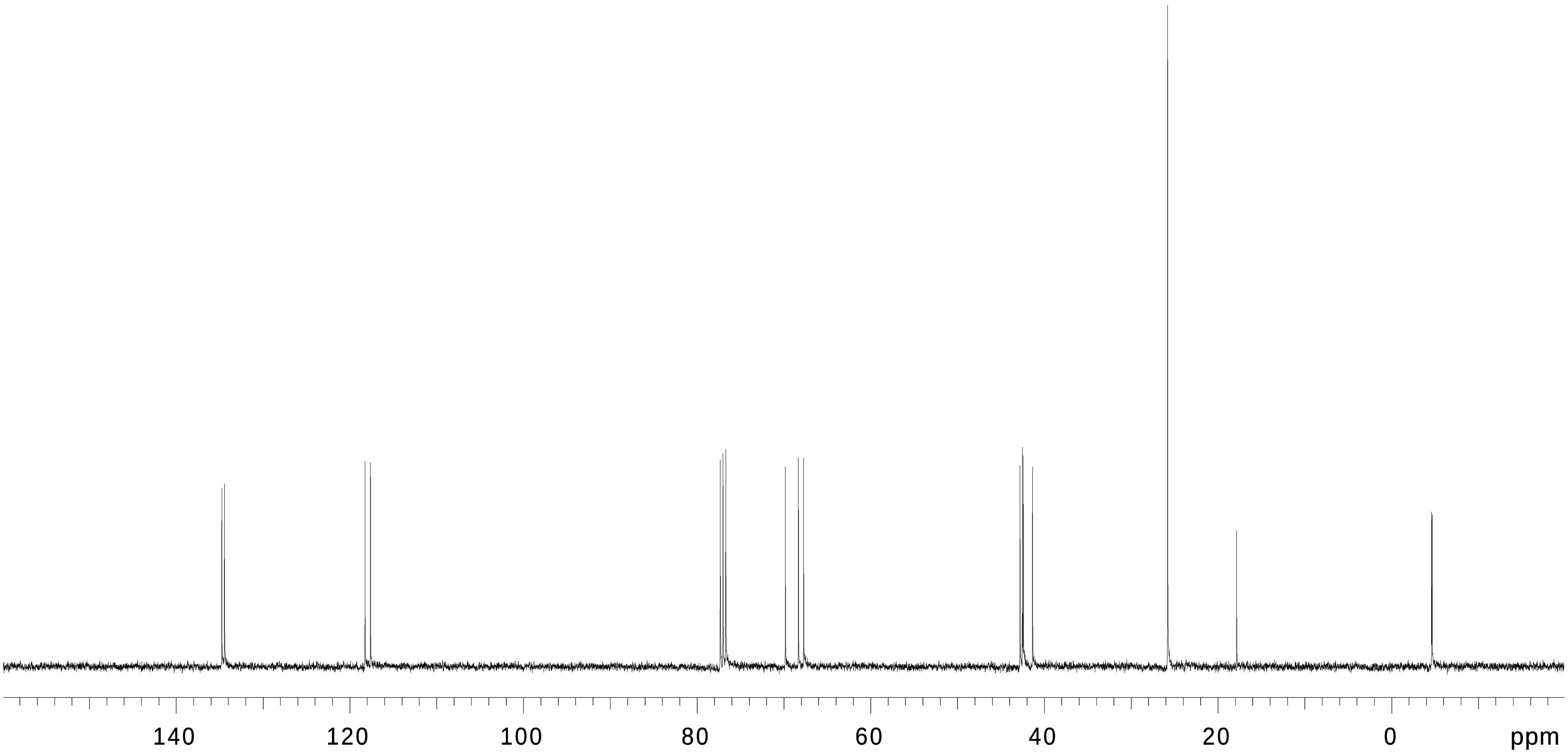
OBSERVE H1, 500.3674490

DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-75-4



15

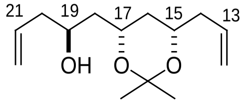


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
229 repetitions

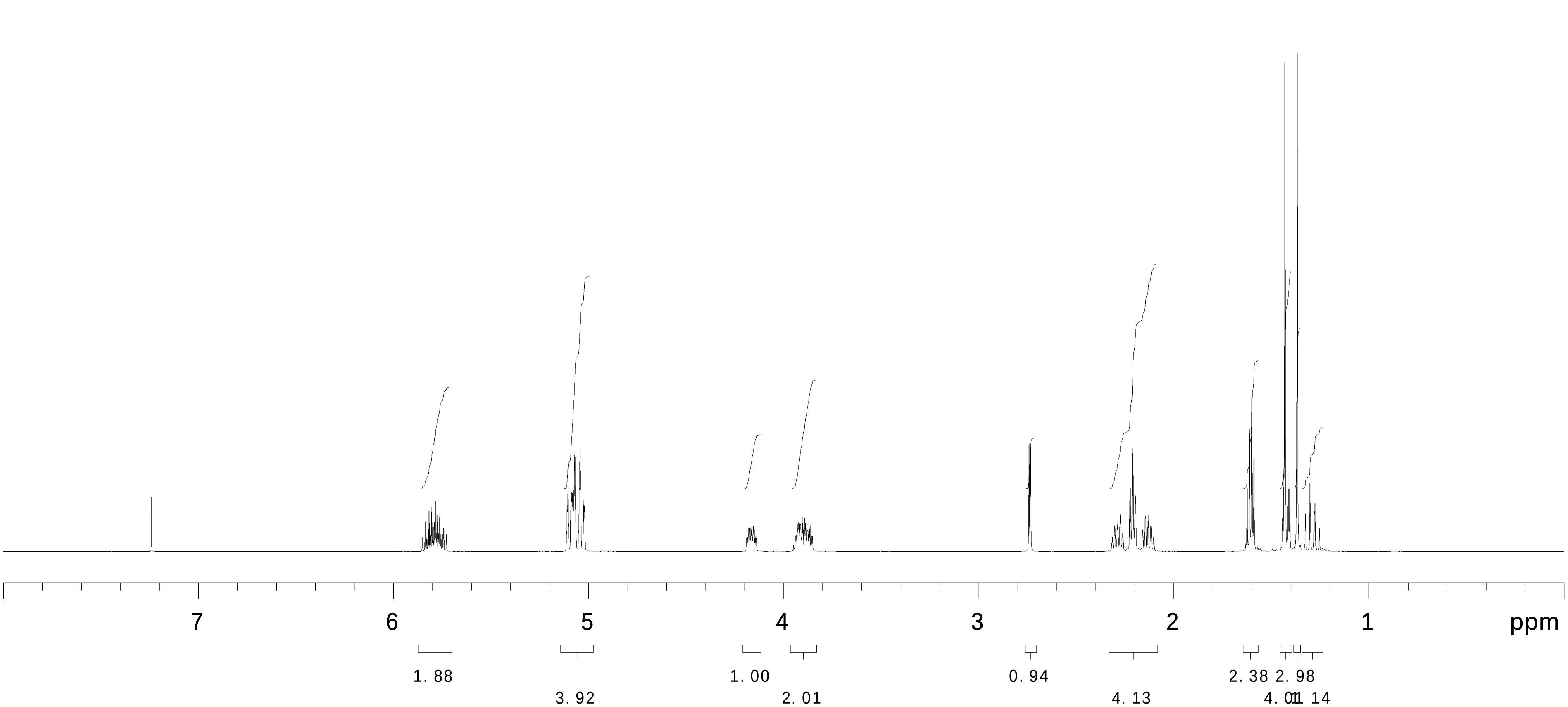
OBSERVE C13, 100.6189883
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 10 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-75-4b



16



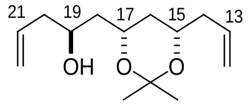
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
32 repetitions

OBSERVE H1, 500.3674490

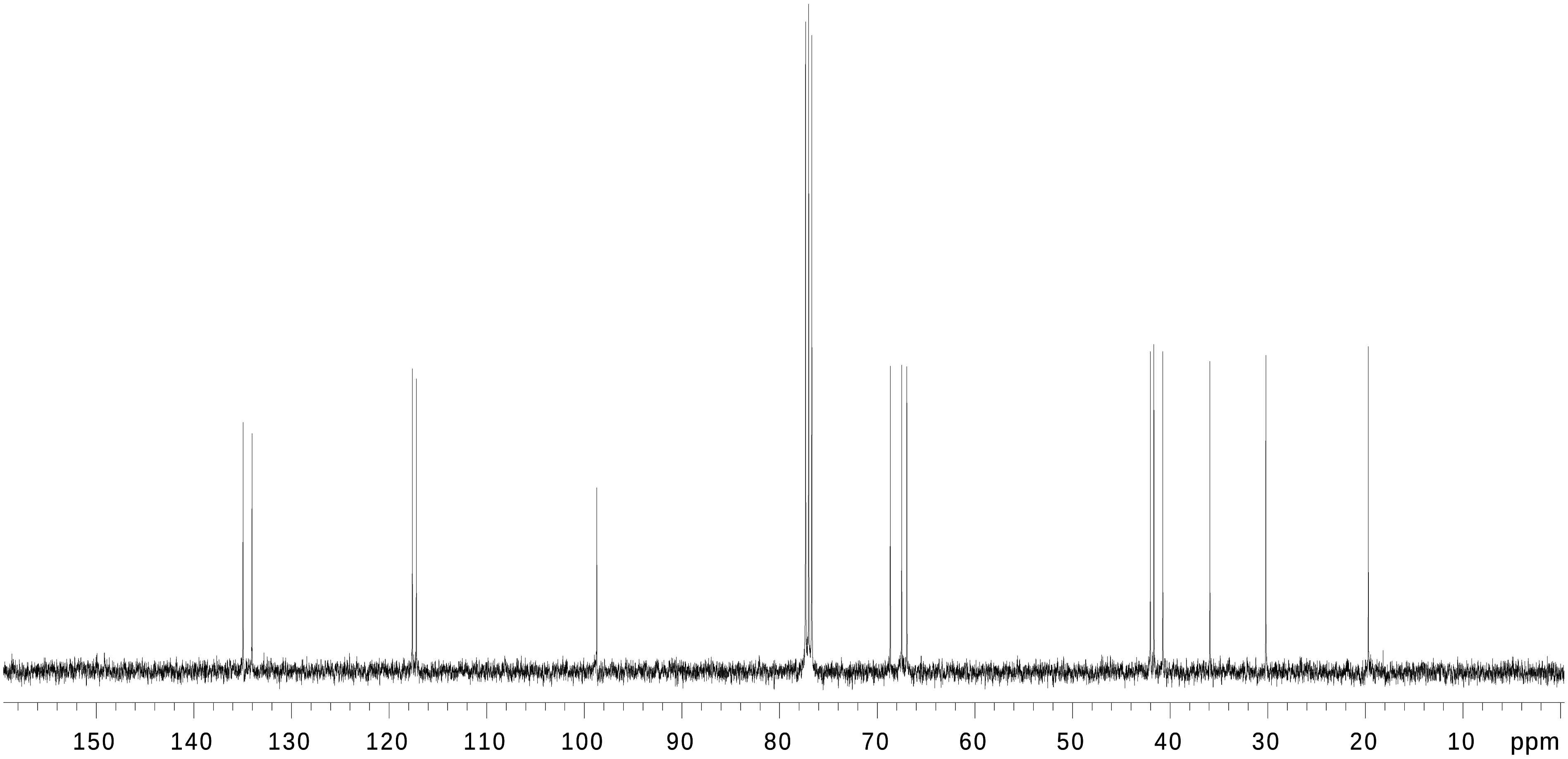
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-81-3

University of Colorado at Boulder NMR



16

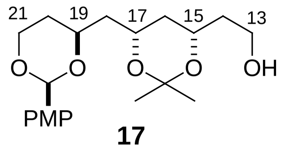


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
338 repetitions

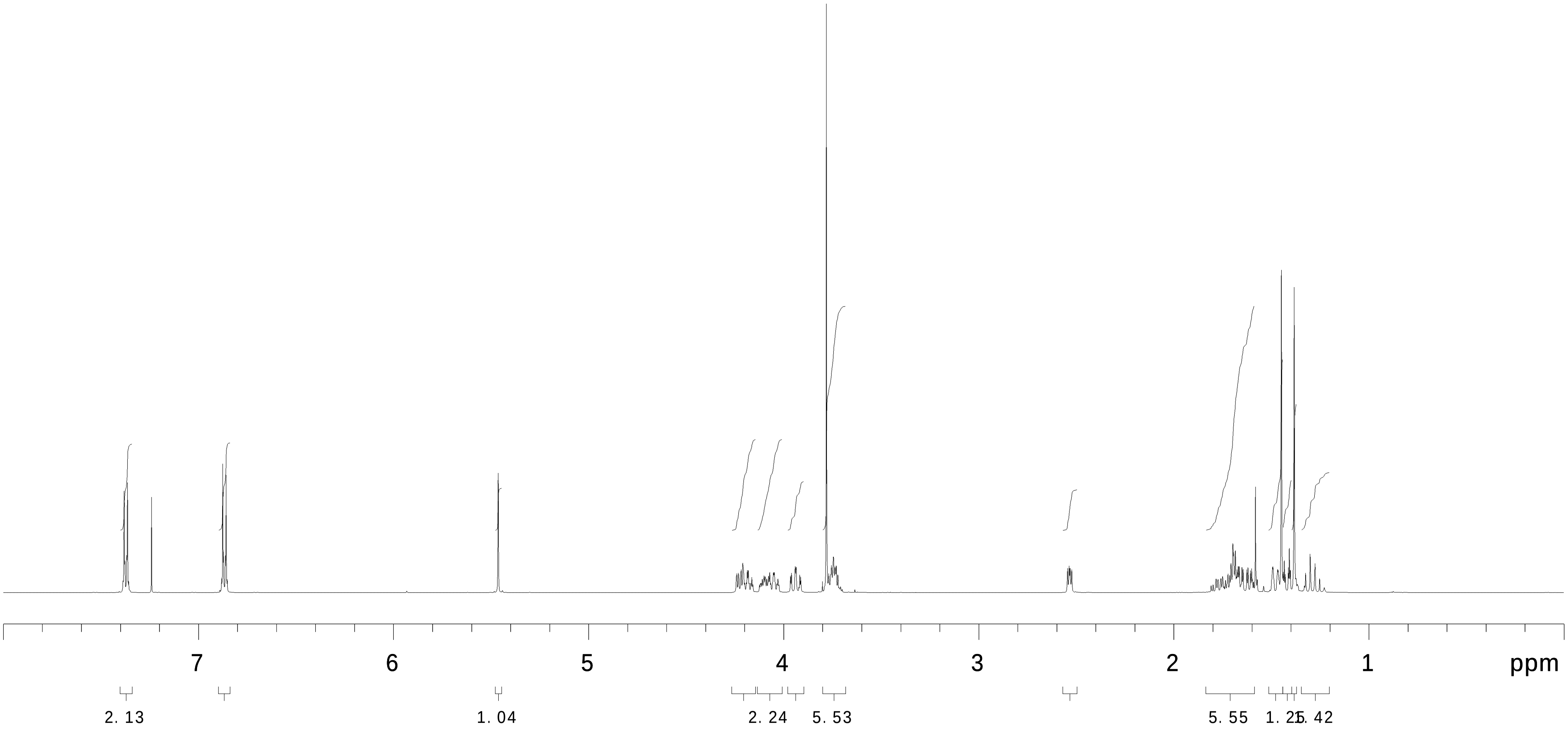
OBSERVE C13, 100.6189868
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 15 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-81-3b



17



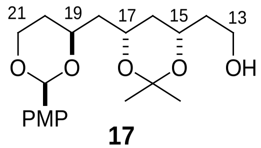
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
64 repetitions

OBSERVE H1, 500.3674490

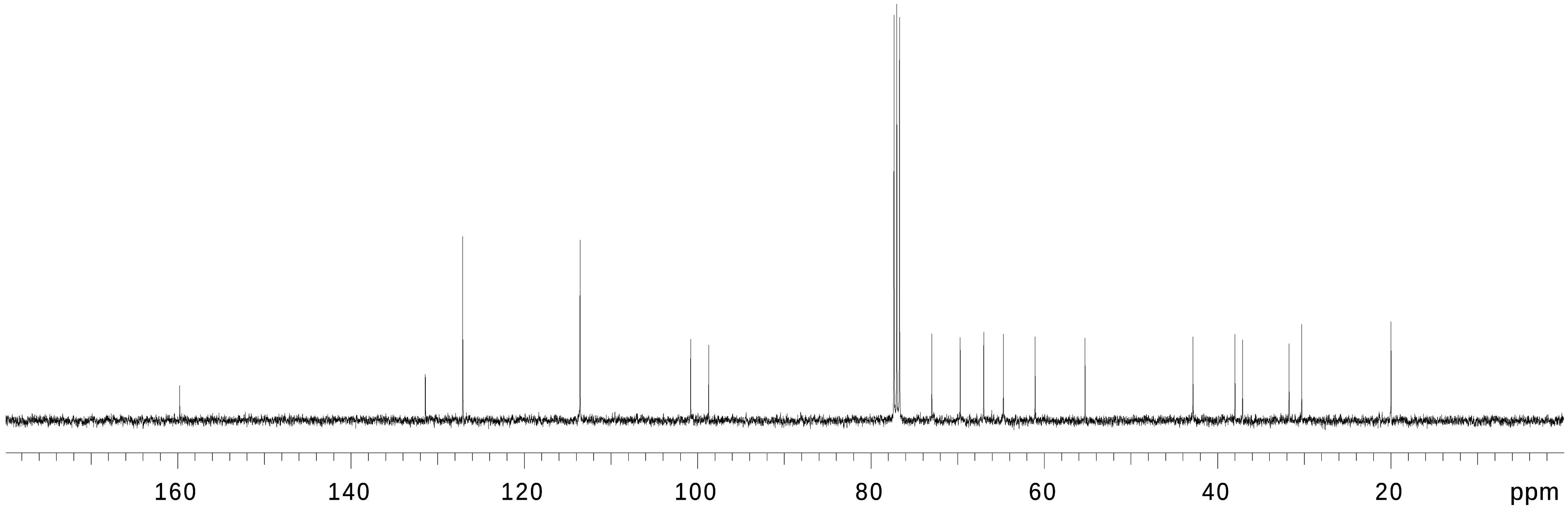
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-84-3

University of Colorado at Boulder NMR



17

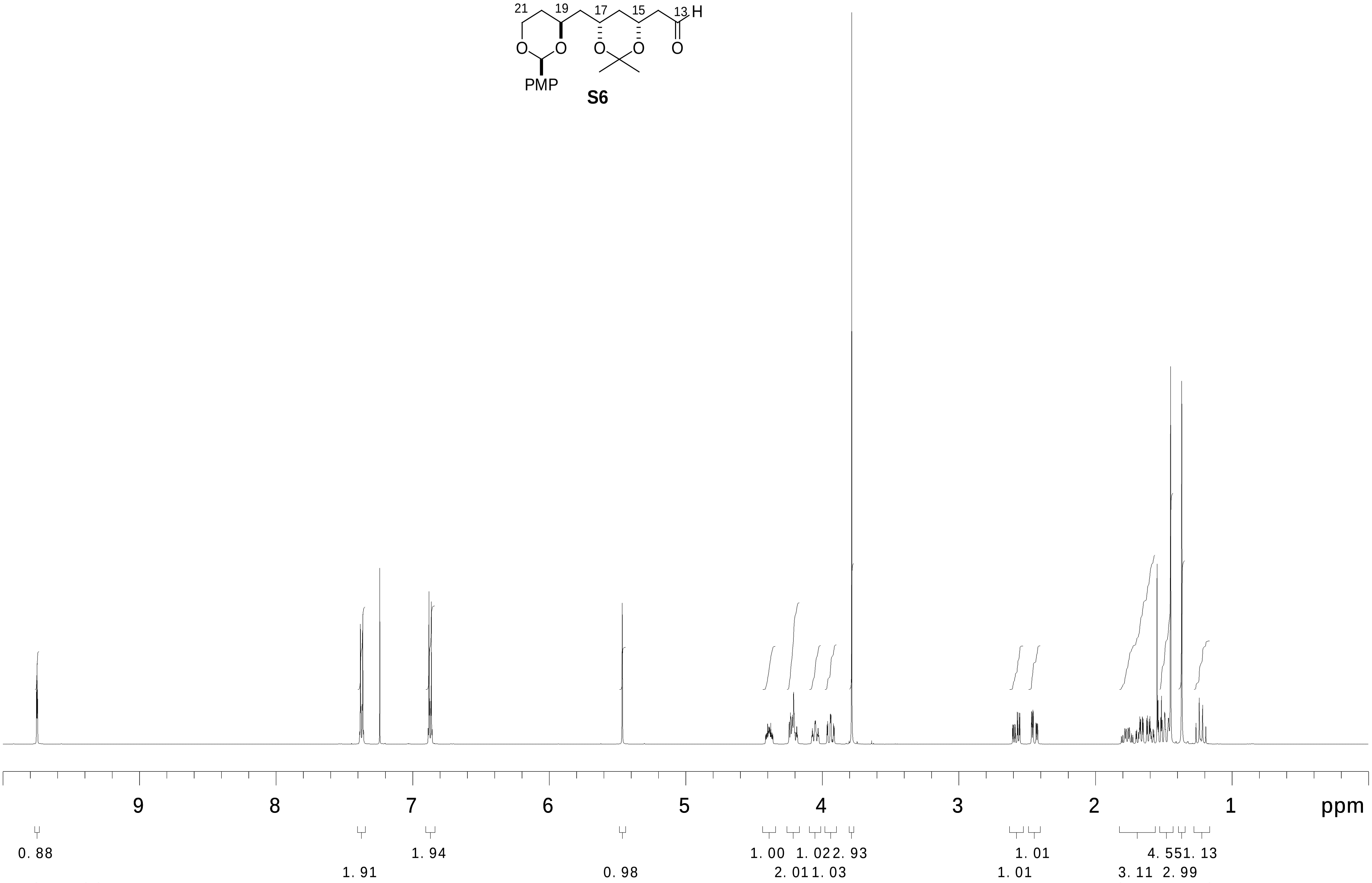


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
608 repetitions

OBSERVE C13, 100.6189872
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 28 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-84-2b



S6

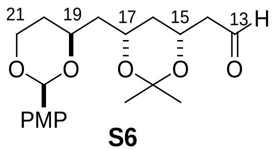
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
64 repetitions

OBSERVE H1, 500.3674488

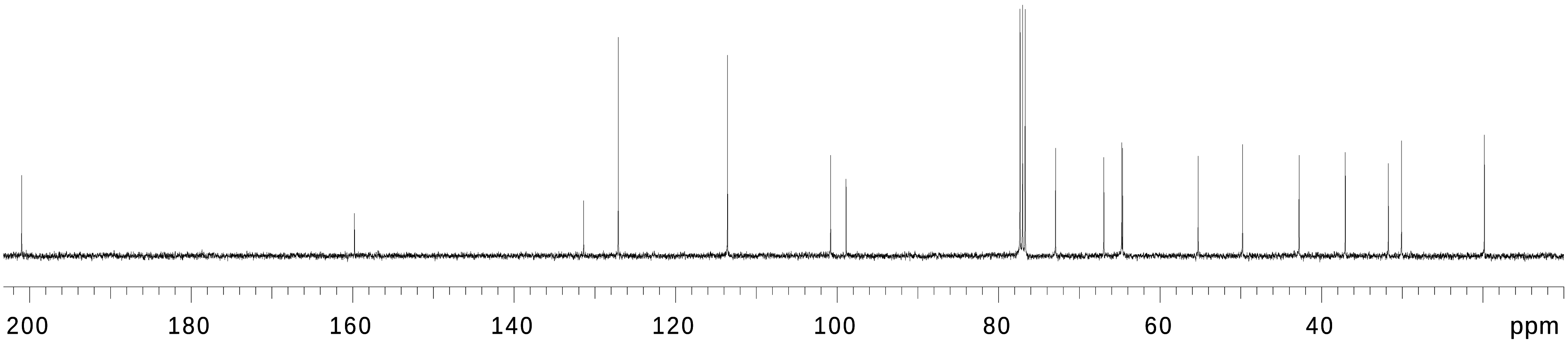
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-86-3

University of Colorado at Boulder NMR



S6

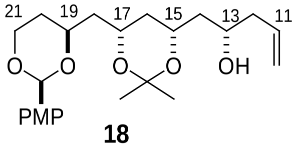


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
514 repetitions

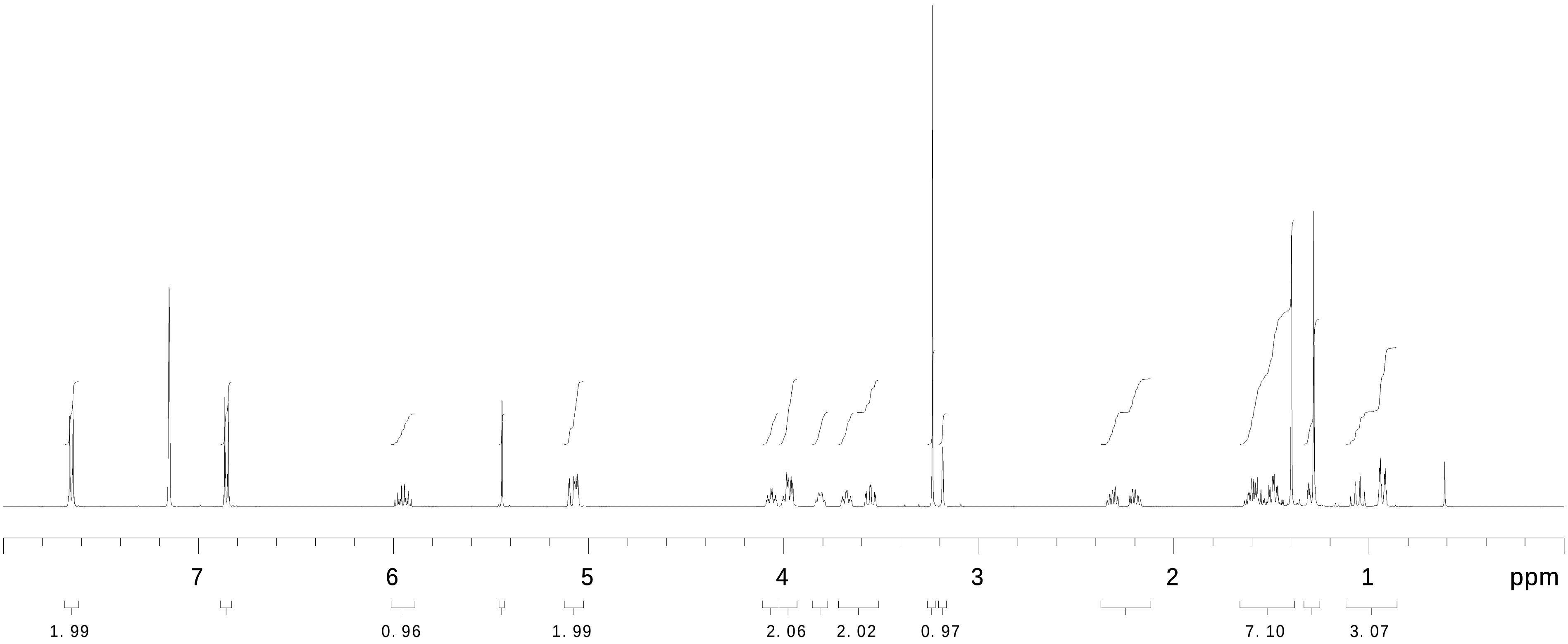
OBSERVE C13, 100.6189883
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 24 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-86-2b



18



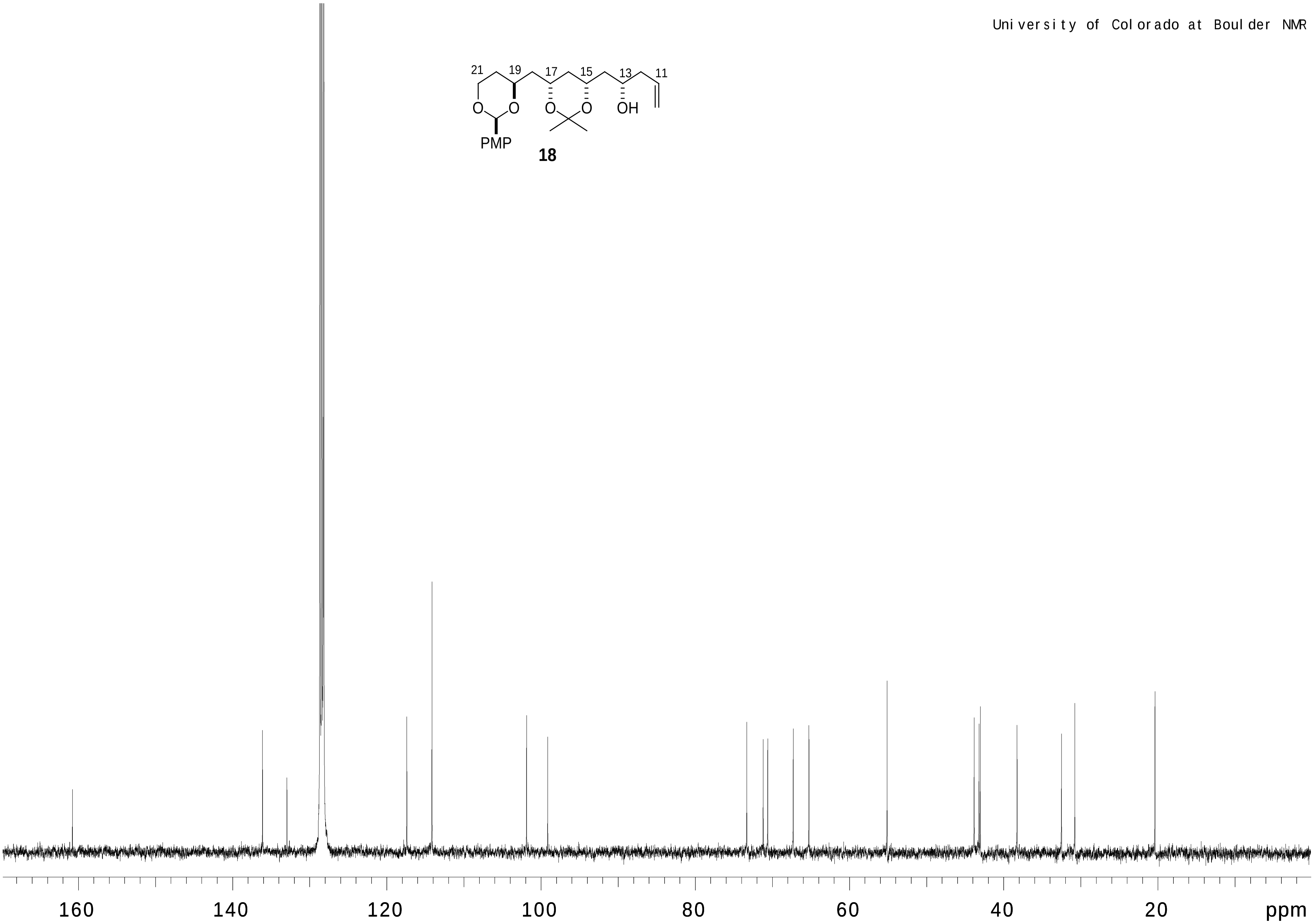
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
27 repetitions

OBSERVE H1, 500.3674678

DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: C6D6
Ambient temperature
File: mjm6-87-3

University of Colorado at Boulder NMR

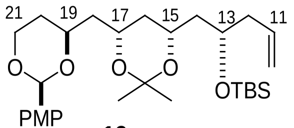


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
583 repetitions

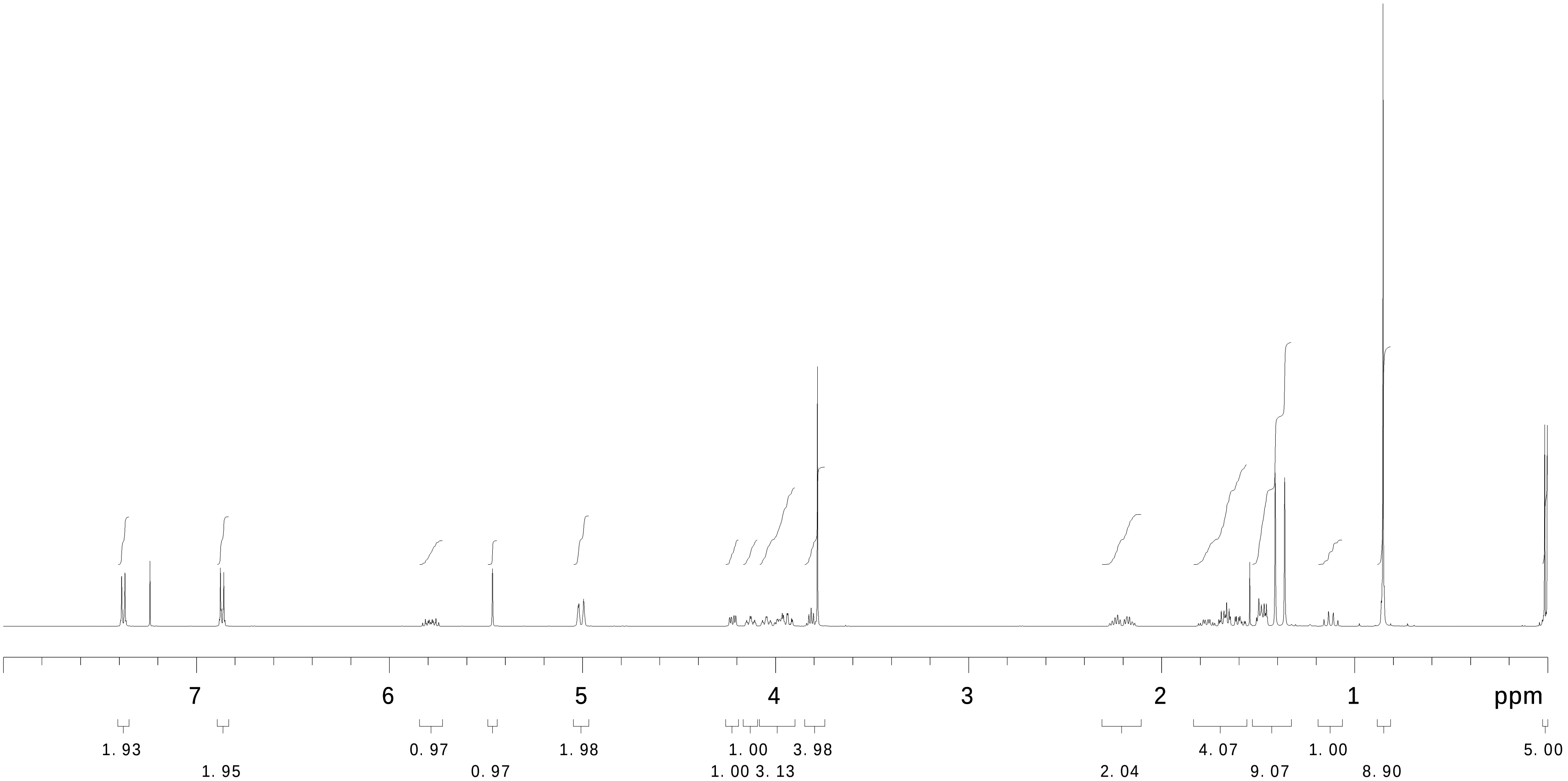
OBSERVE C13, 100.6189204
DECOUPLE H1, 400.1575167
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 27 minutes

Solvent: C6D6
Ambient temperature
File: mjm6-87-3b



19



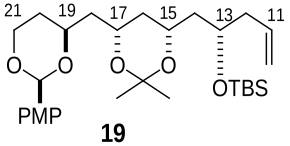
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
66 repetitions

OBSERVE H1, 500.3674491

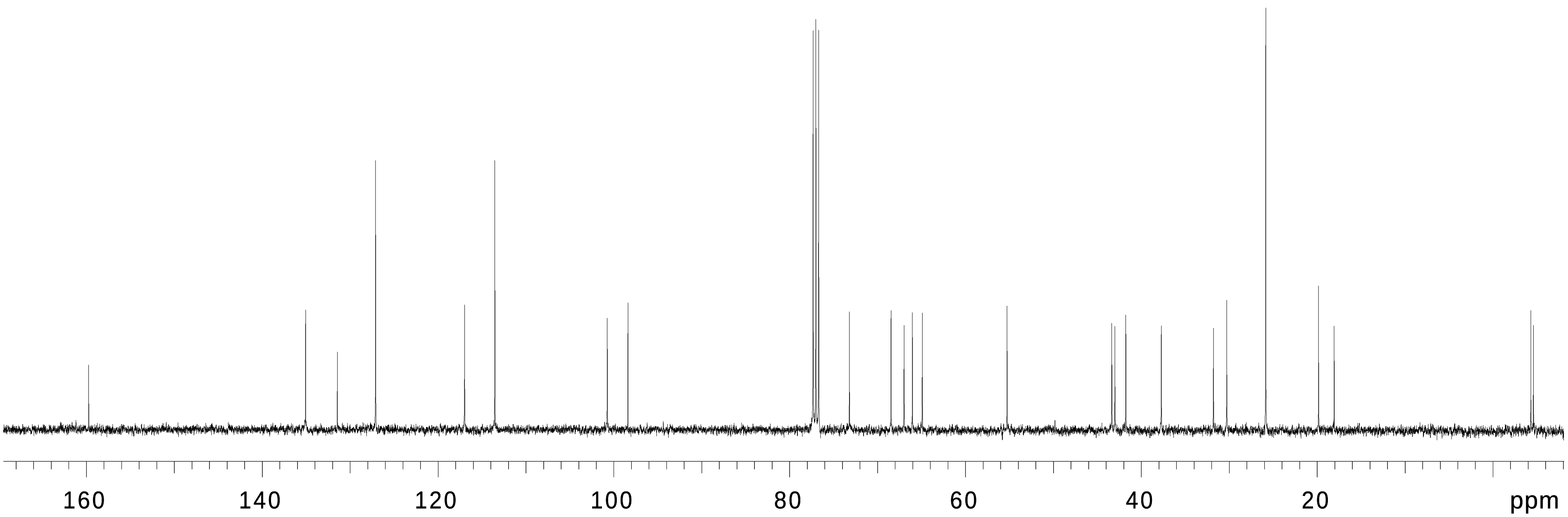
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-90-3

University of Colorado at Boulder NMR



19



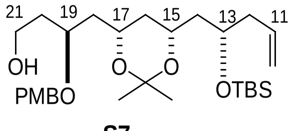
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
480 repetitions

OBSERVE C13, 100.6189887
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

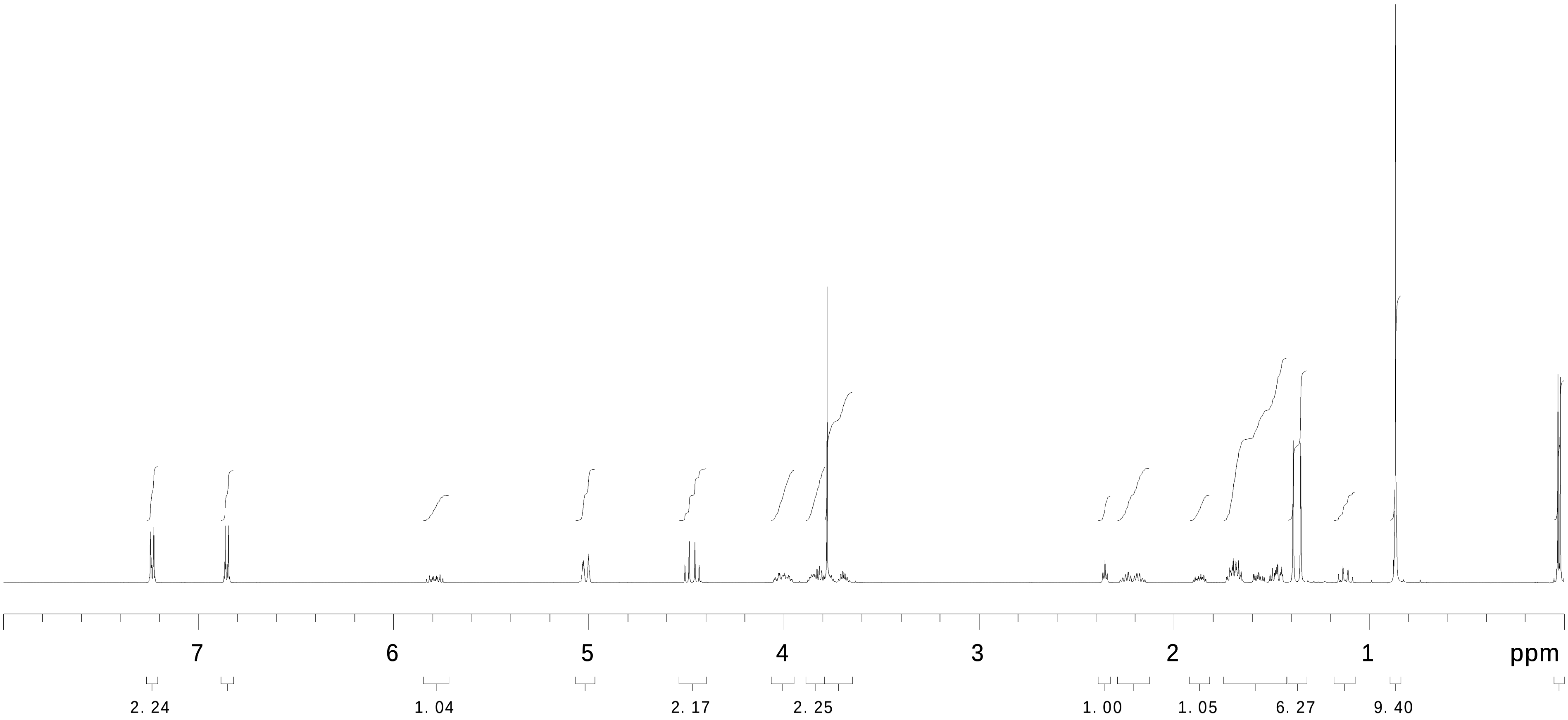
DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 22 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-90-3b

University of Colorado at Boulder NMR



S7



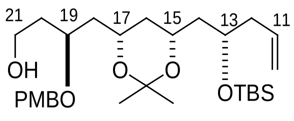
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
16 repetitions

OBSERVE H1, 500.3674488

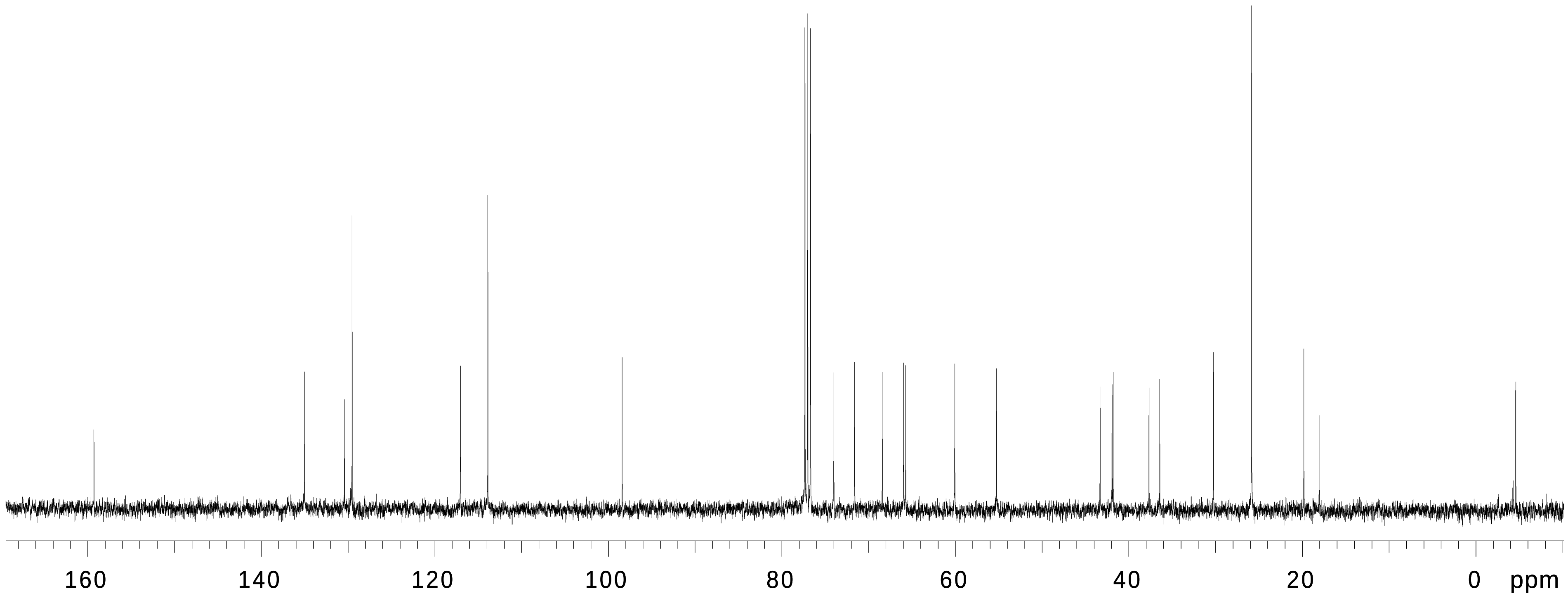
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-92-3

University of Colorado at Boulder NMR



S7

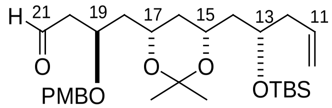


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
272 repetitions

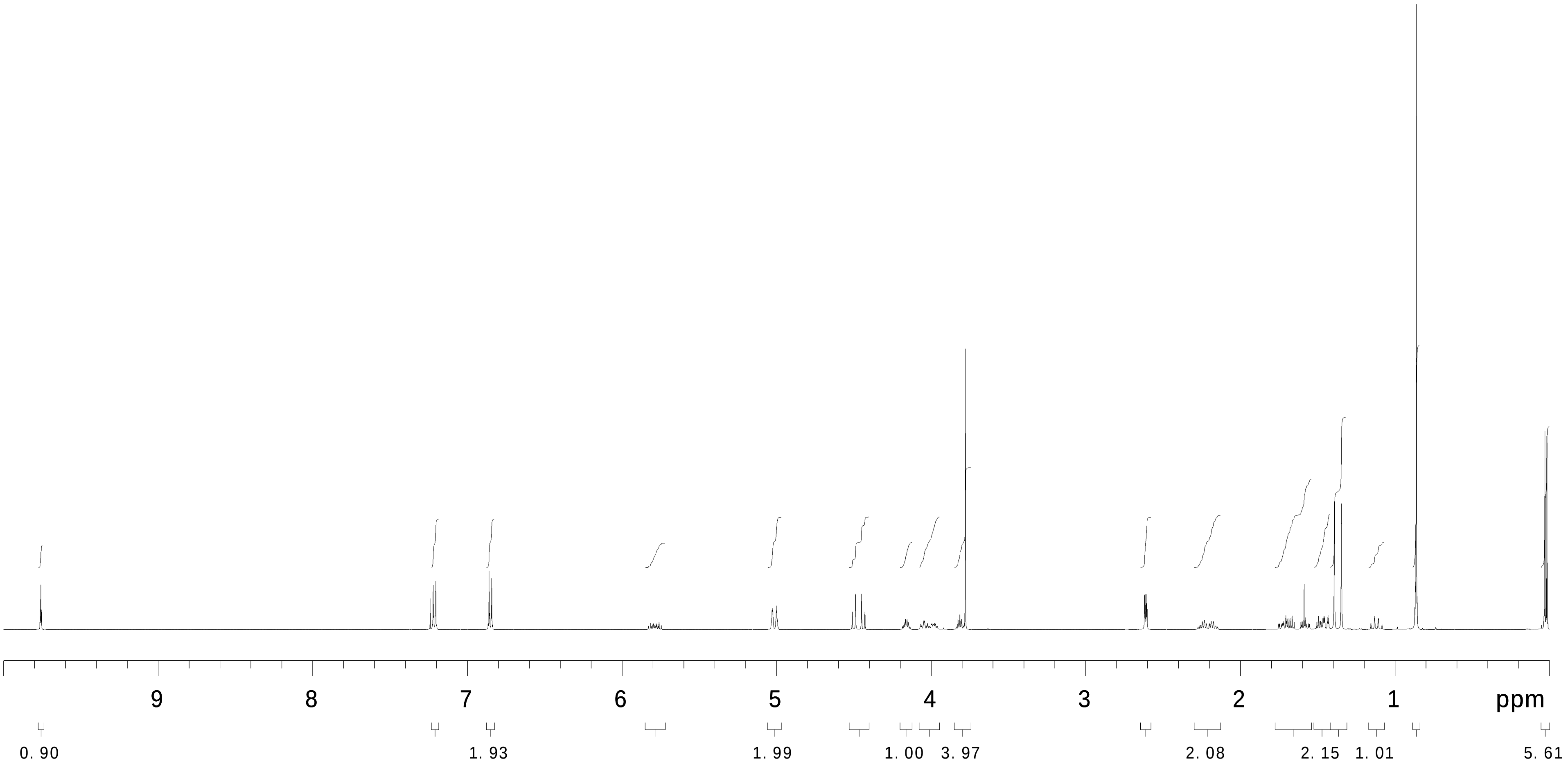
OBSERVE C13, 100.6189887
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 12 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-92-3b



3



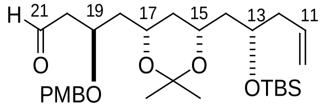
Relax. delay 0.100 sec
Pulse 29.1 degrees
Acq. time 3.000 sec
Width 6505.1 Hz
17 repetitions

OBSERVE H1, 500.3674488

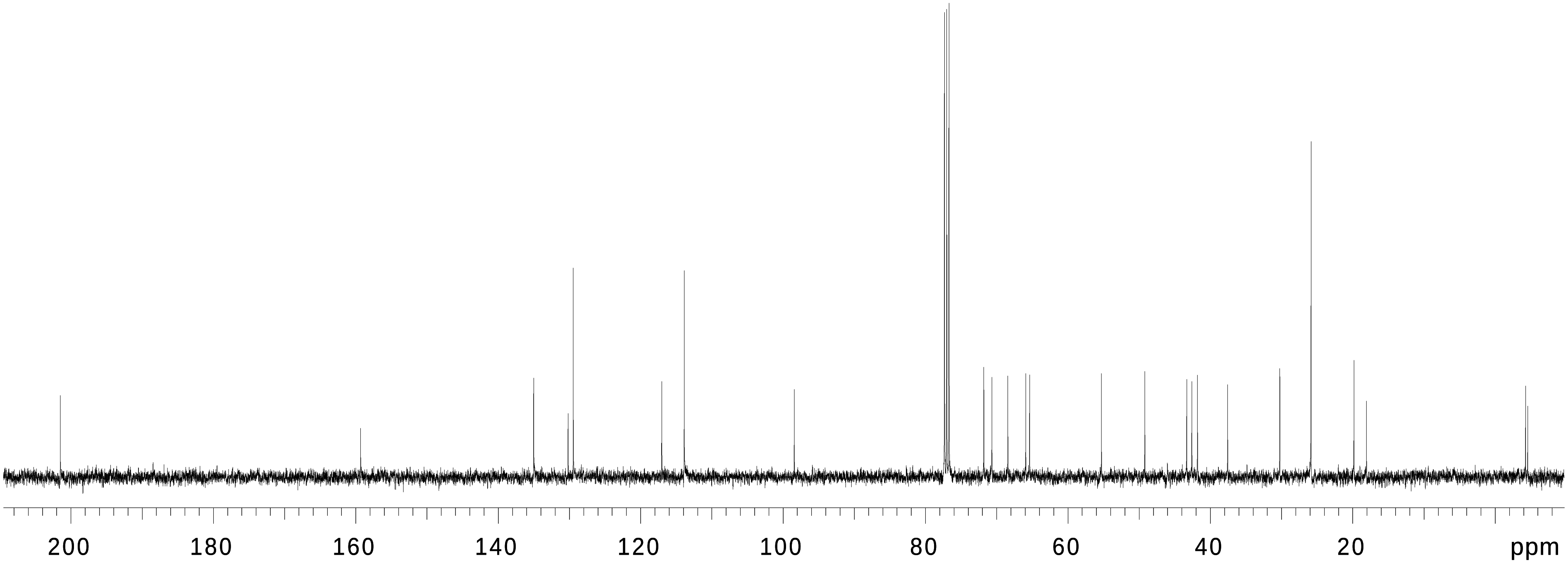
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: mjm6-128-2

University of Colorado at Boulder NMR



3

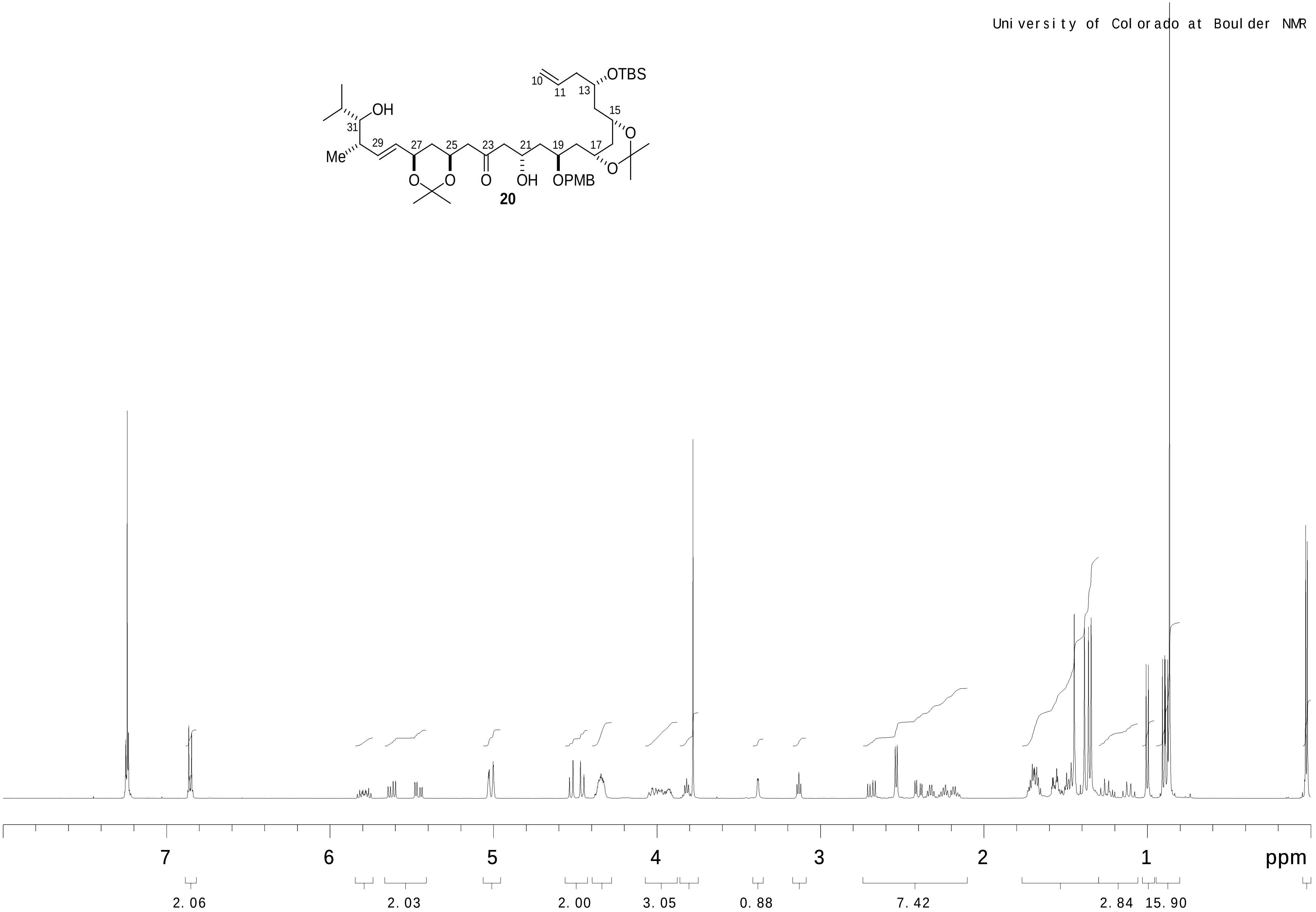


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
390 repetitions

OBSERVE C13, 100.6189872
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 18 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-128-2b



20

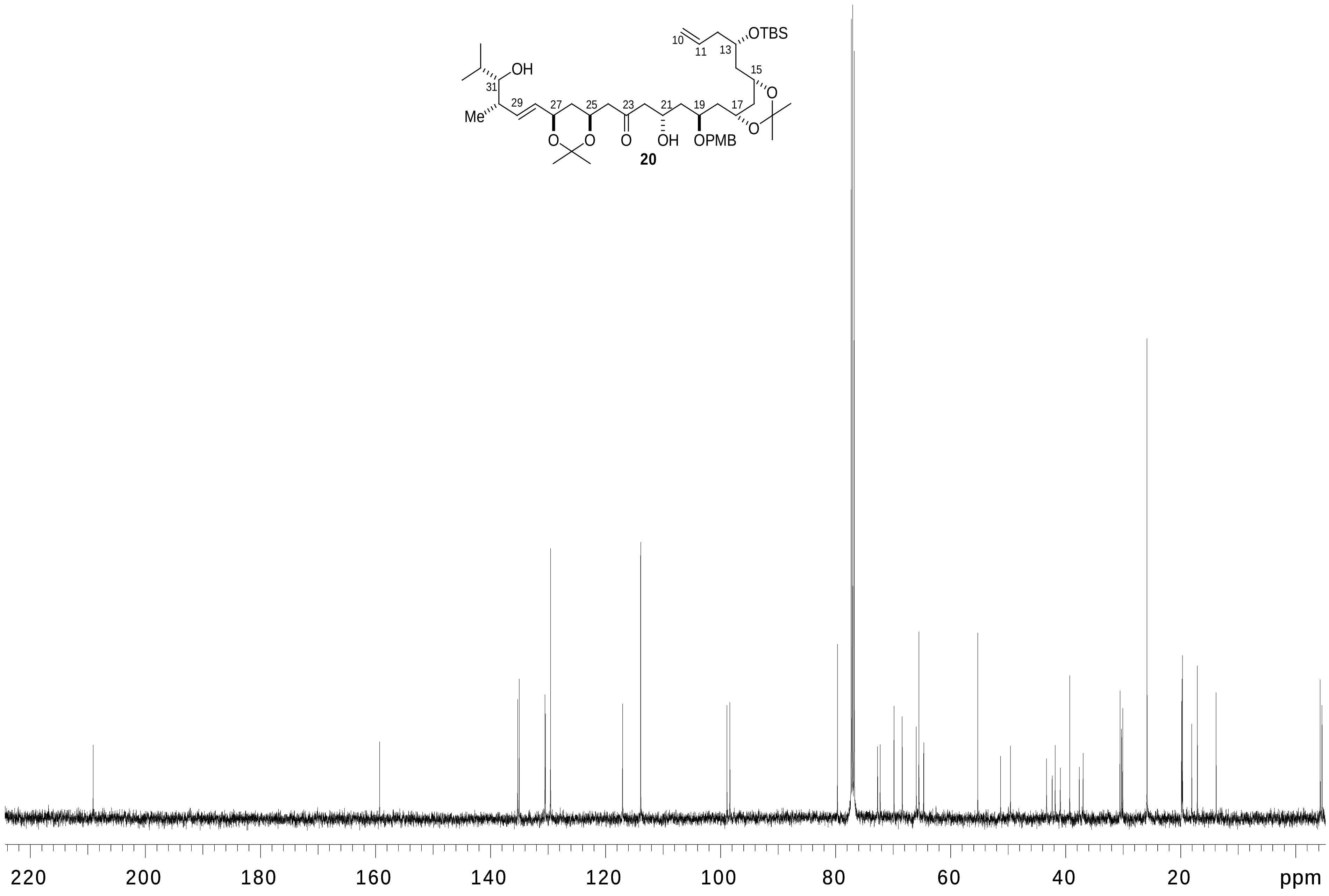
Relax. delay 1.500 sec
Pulse 20.8 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
45 repetitions

OBSERVE H1, 500.3674486

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-093-n2-proto

University of Colorado at Boulder NMR



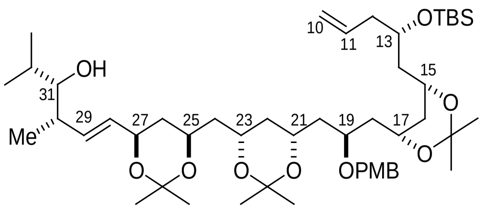
Relax. delay 1.000 sec
Pulse 32.6 degrees
Acq. time 1.134 sec
Width 28891.3 Hz
1024 repetitions

OBSERVE C13, 125.8174949
DECOUPLE H1, 500.3697761
Power 44 dB
on during acquisition
off during delay
WALTZ-16 modulated

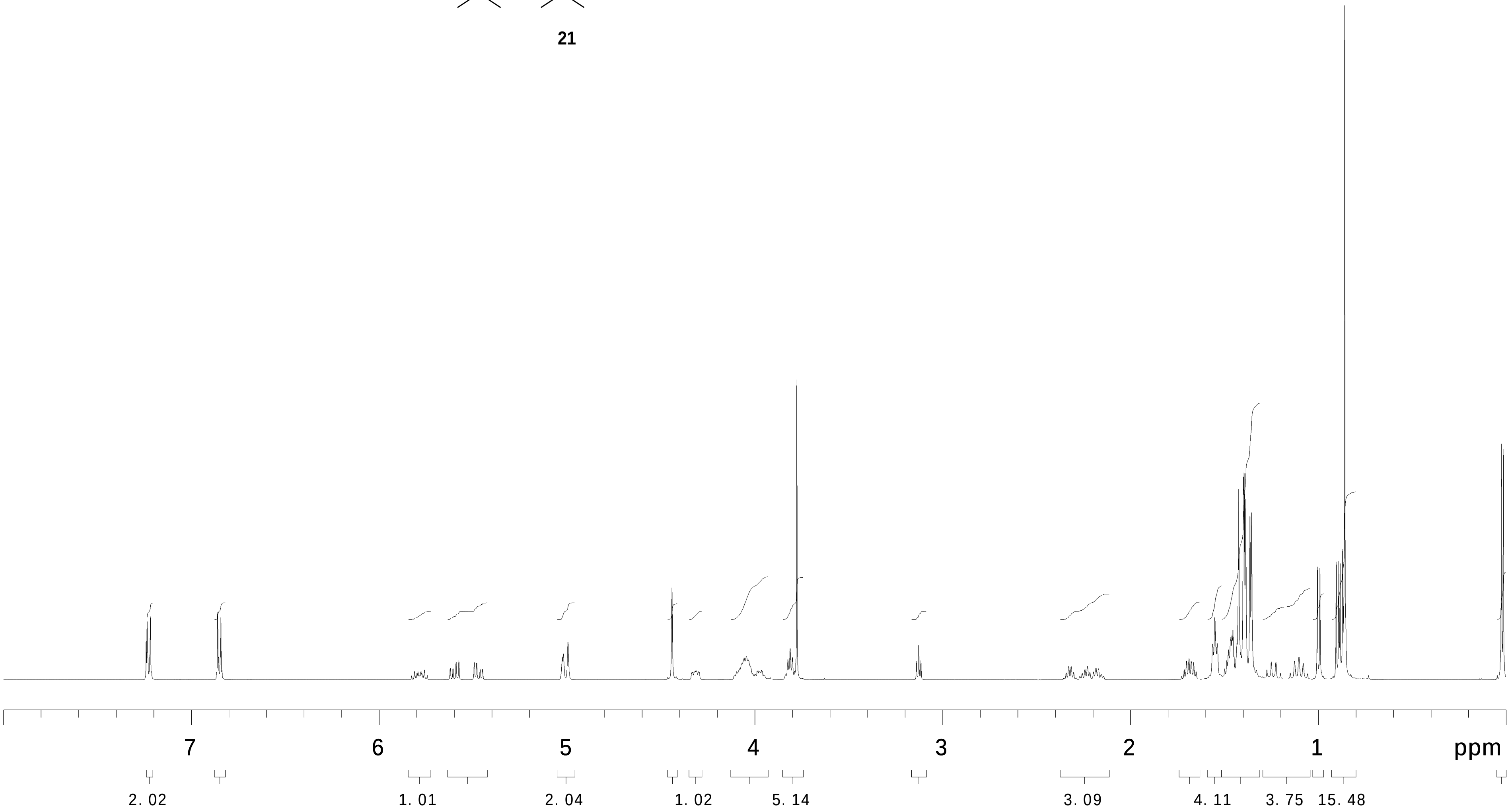
DATA PROCESSING
Line broadening 1.2 Hz
FT size 65536
Total time 36 minutes

Solvent: CDCl3
Ambient temperature
File: mjm6-139-4a

University of Colorado at Boulder NMR



21



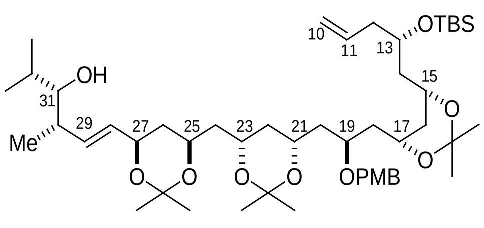
Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
33 repetitions

OBSERVE H1, 500.3674487

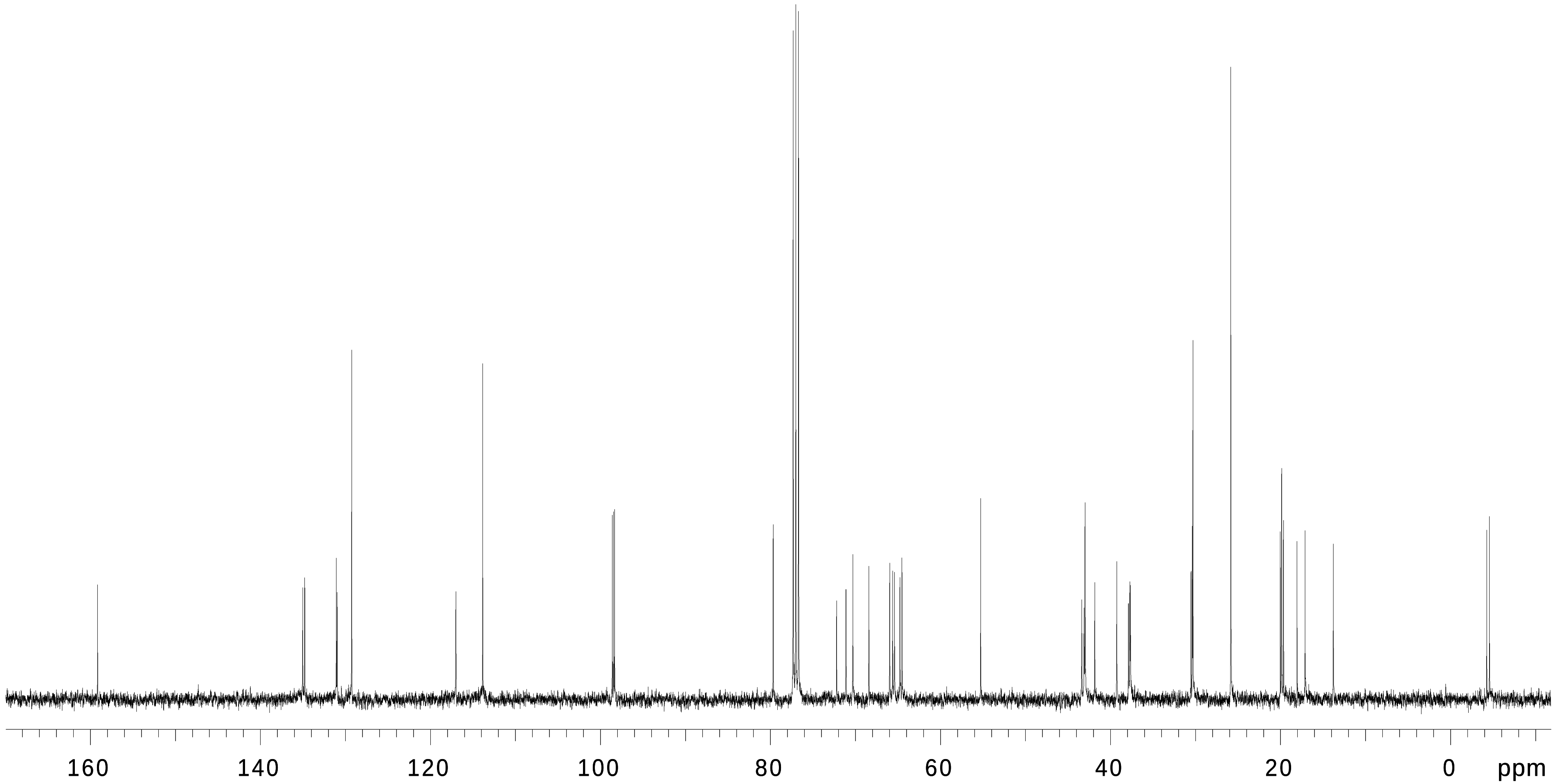
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 2 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-050-n2-proto

University of Colorado at Boulder NMR



21

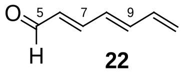


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
513 repetitions

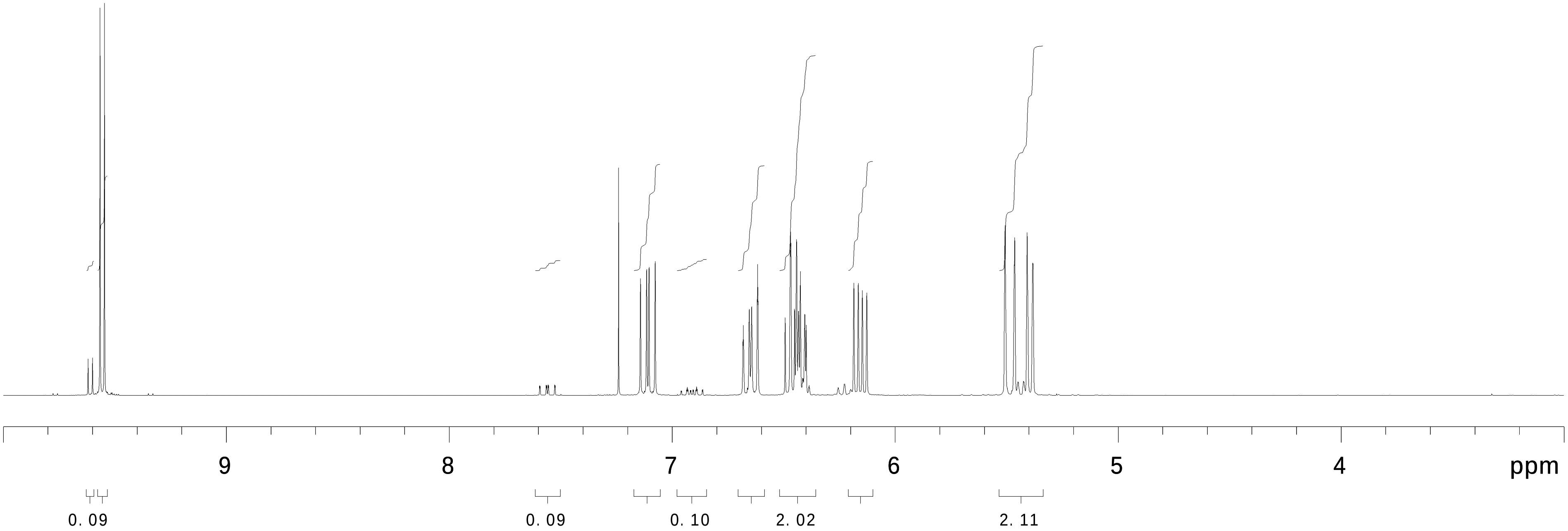
OBSERVE C13, 100.6189882
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 24 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-050-2-carbon



22



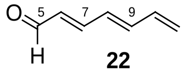
Relax. delay 1.500 sec
Pulse 35.0 degrees
Acq. time 2.999 sec
Width 6002.4 Hz
41 repetitions

OBSERVE H1, 400.1547356

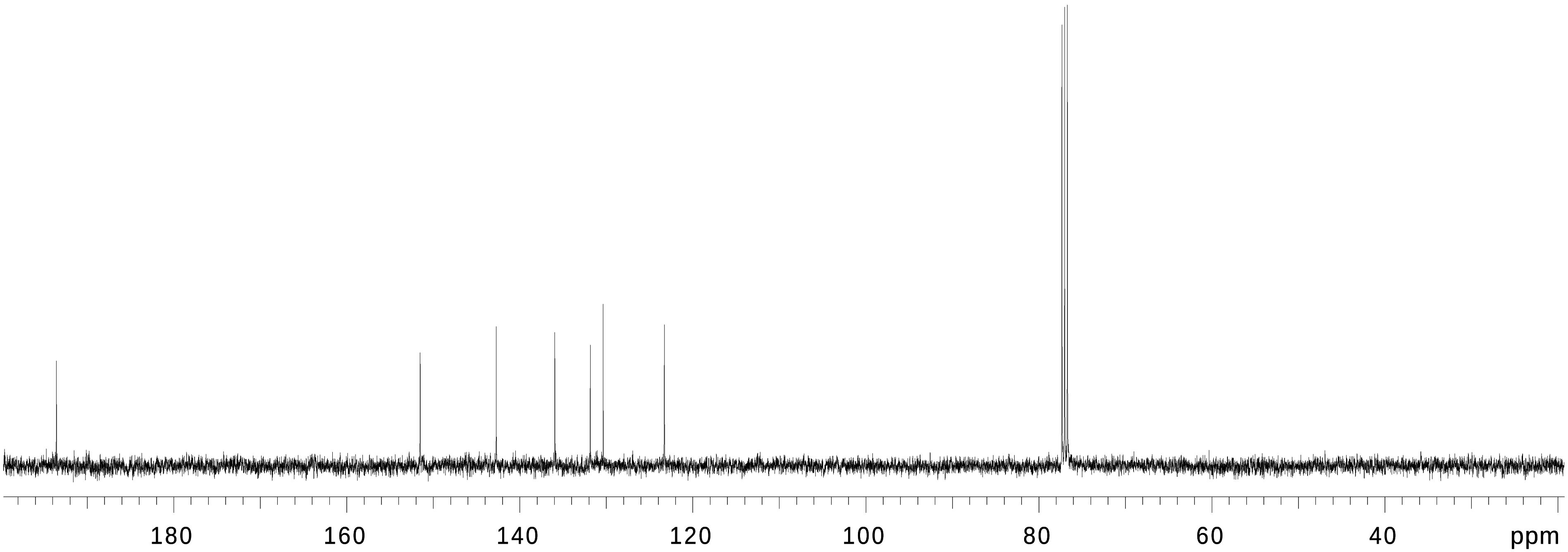
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 3 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-070-1proton

University of Colorado at Boulder NMR



22



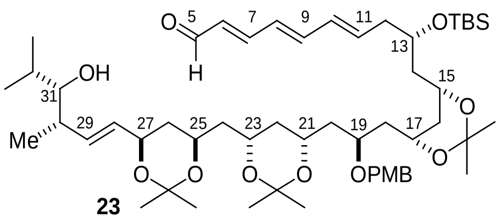
Relax. delay 1.500 sec
Pulse 40.3 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
145 repetitions

OBSERVE C13, 100.6189878
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

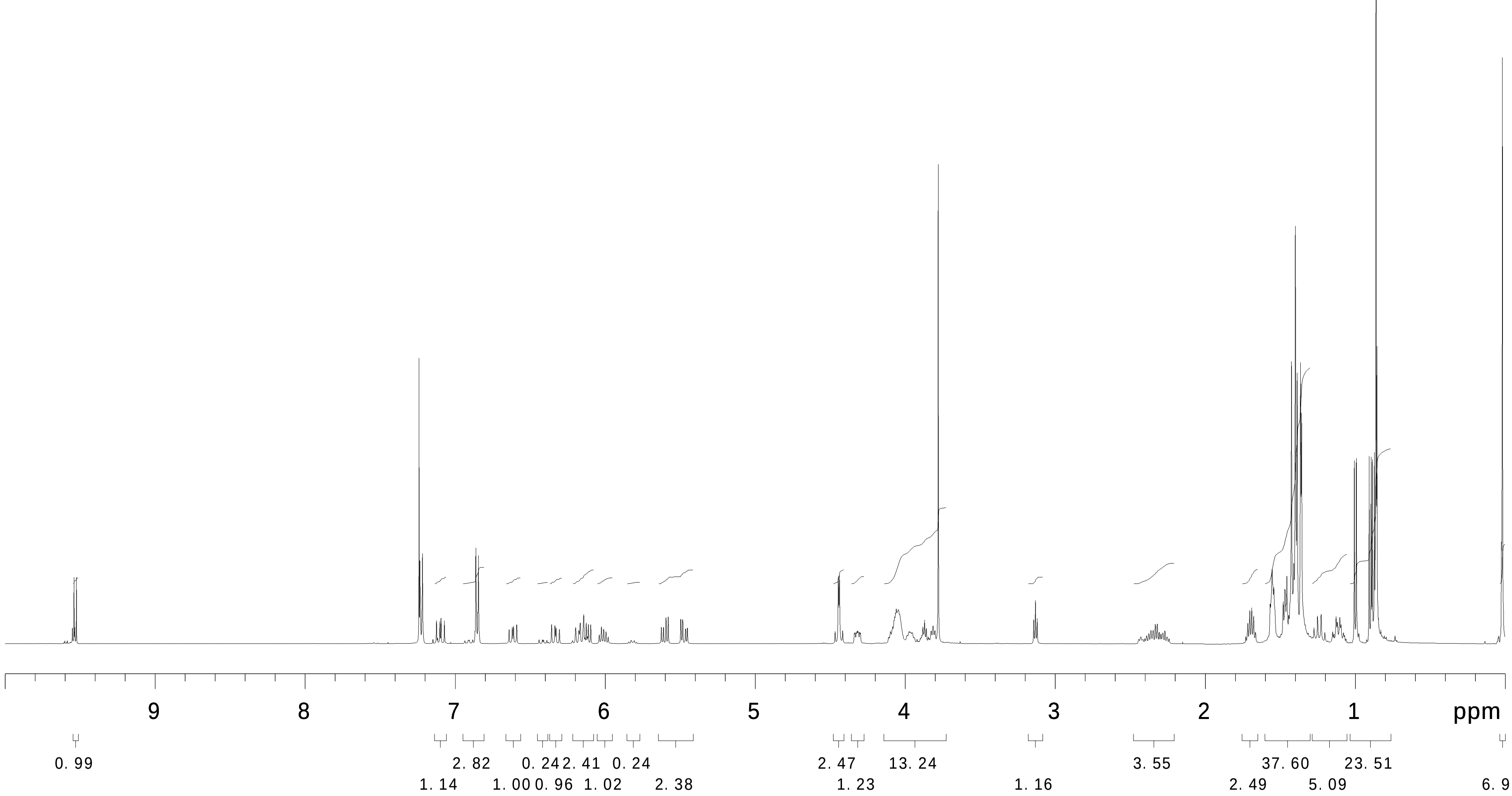
DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 6 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-070-n1carbo

University of Colorado at Boulder NMR



23



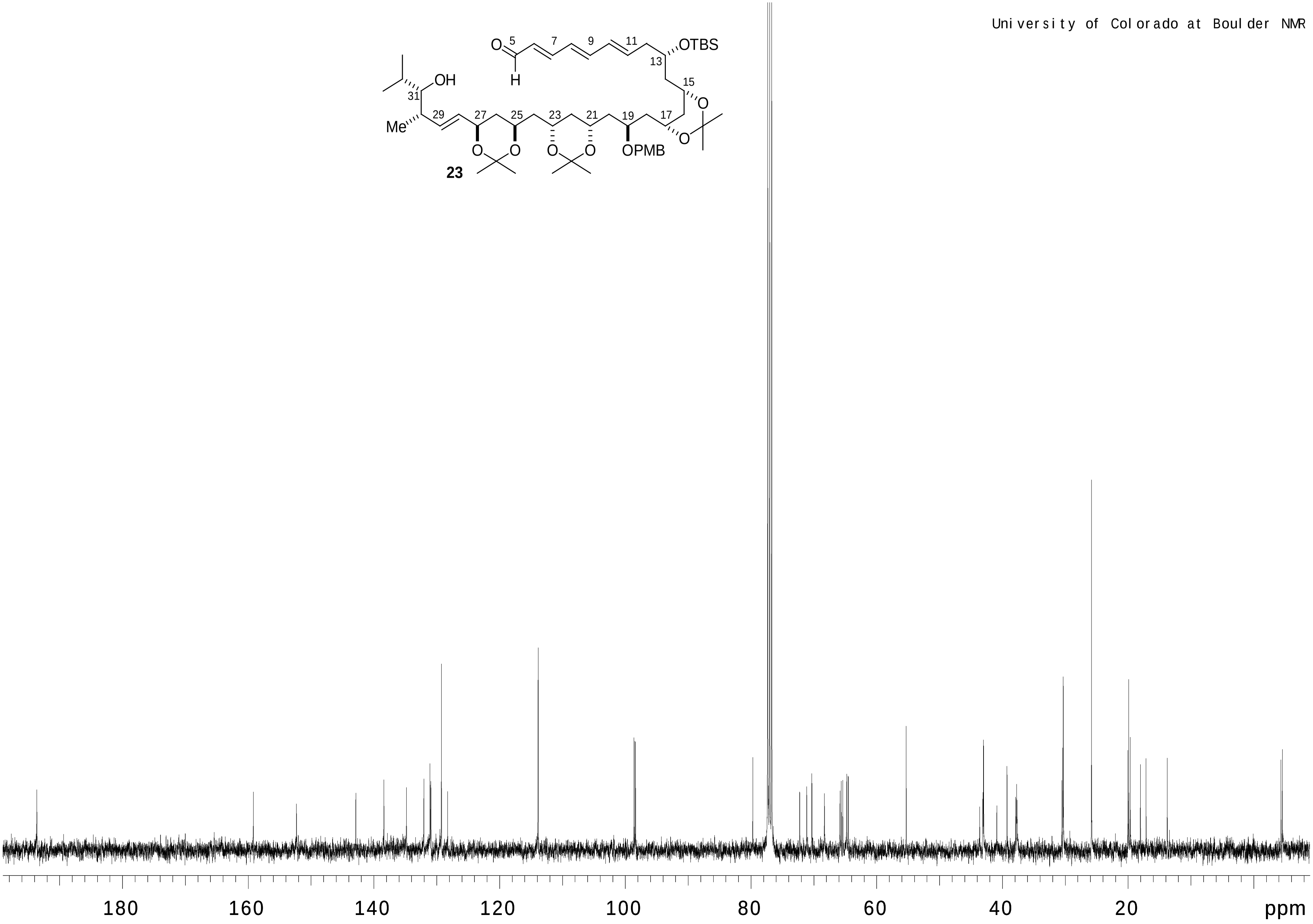
Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
81 repetitions

OBSERVE H1, 500.3674486

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 6 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-054-n2-proto

University of Colorado at Boulder NMR

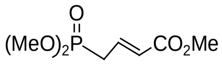


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
1128 repetitions

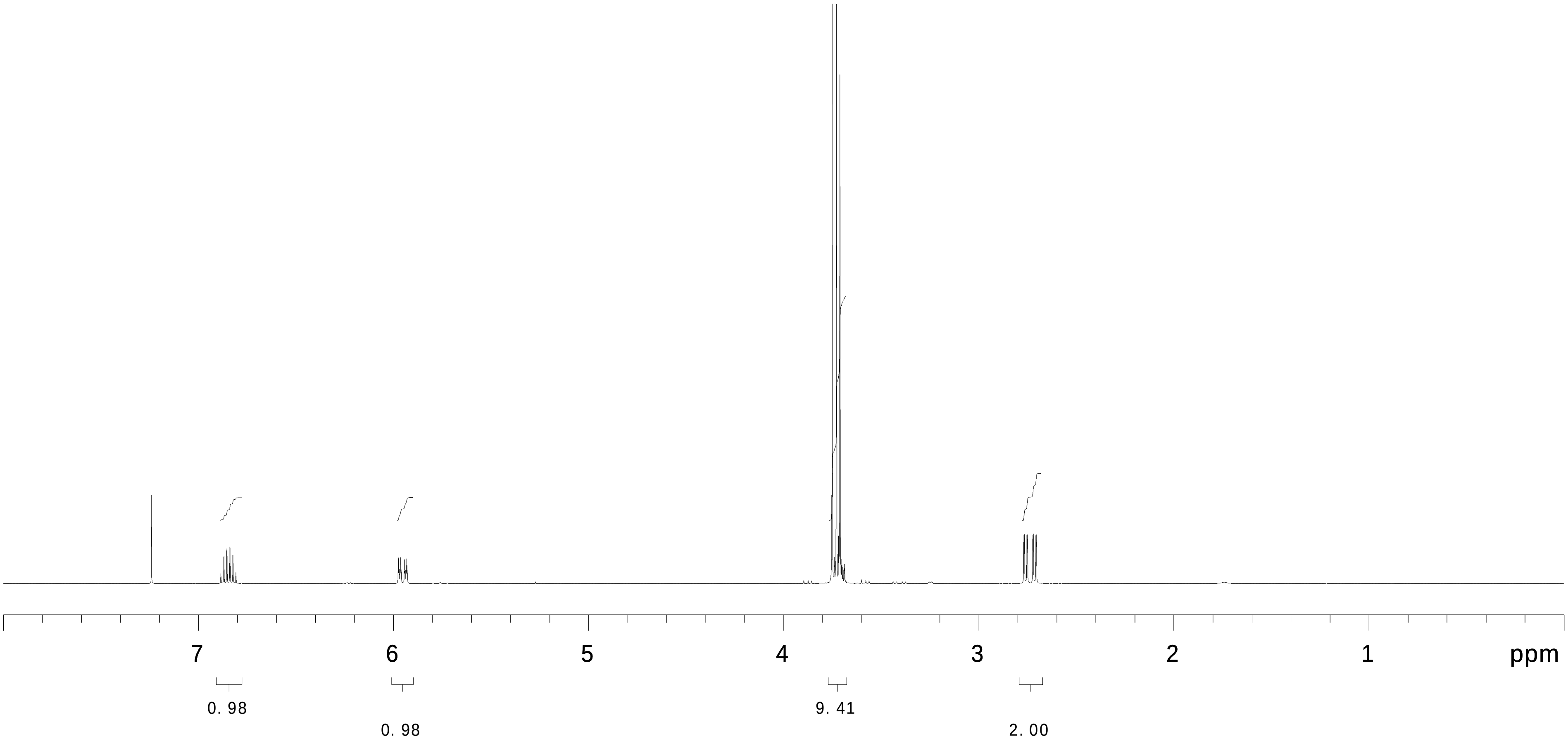
OBSERVE C13, 100.6189870
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 52 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-054-n2carbo



24



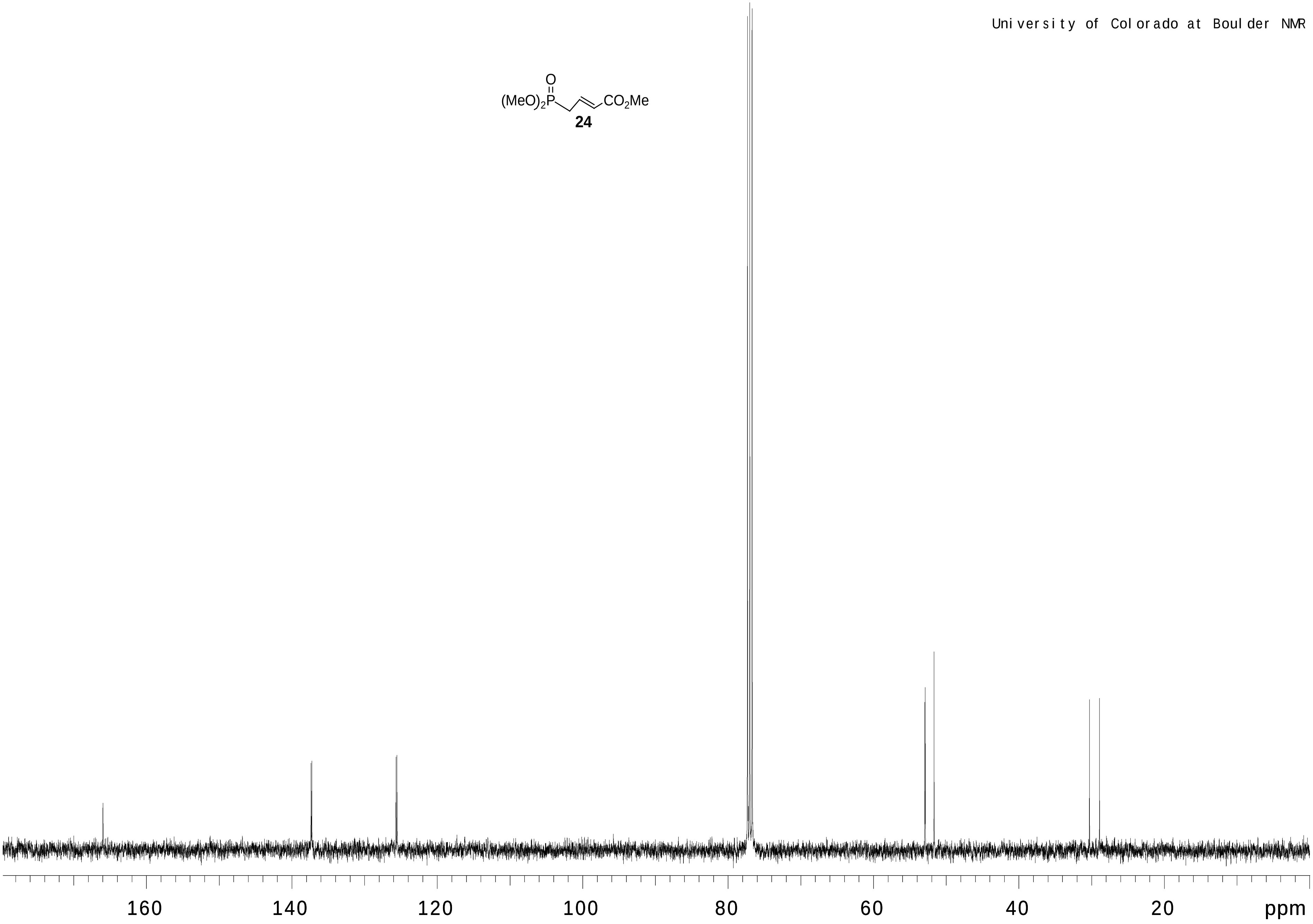
Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
65 repetitions

OBSERVE H1, 500.3674486

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-075-m2-proto

University of Colorado at Boulder NMR



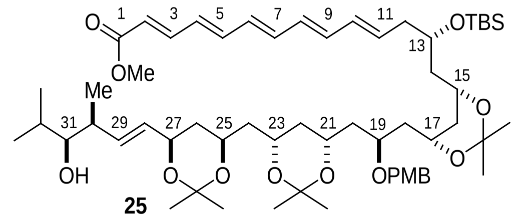
24

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.309 sec
Width 25039.1 Hz
466 repetitions

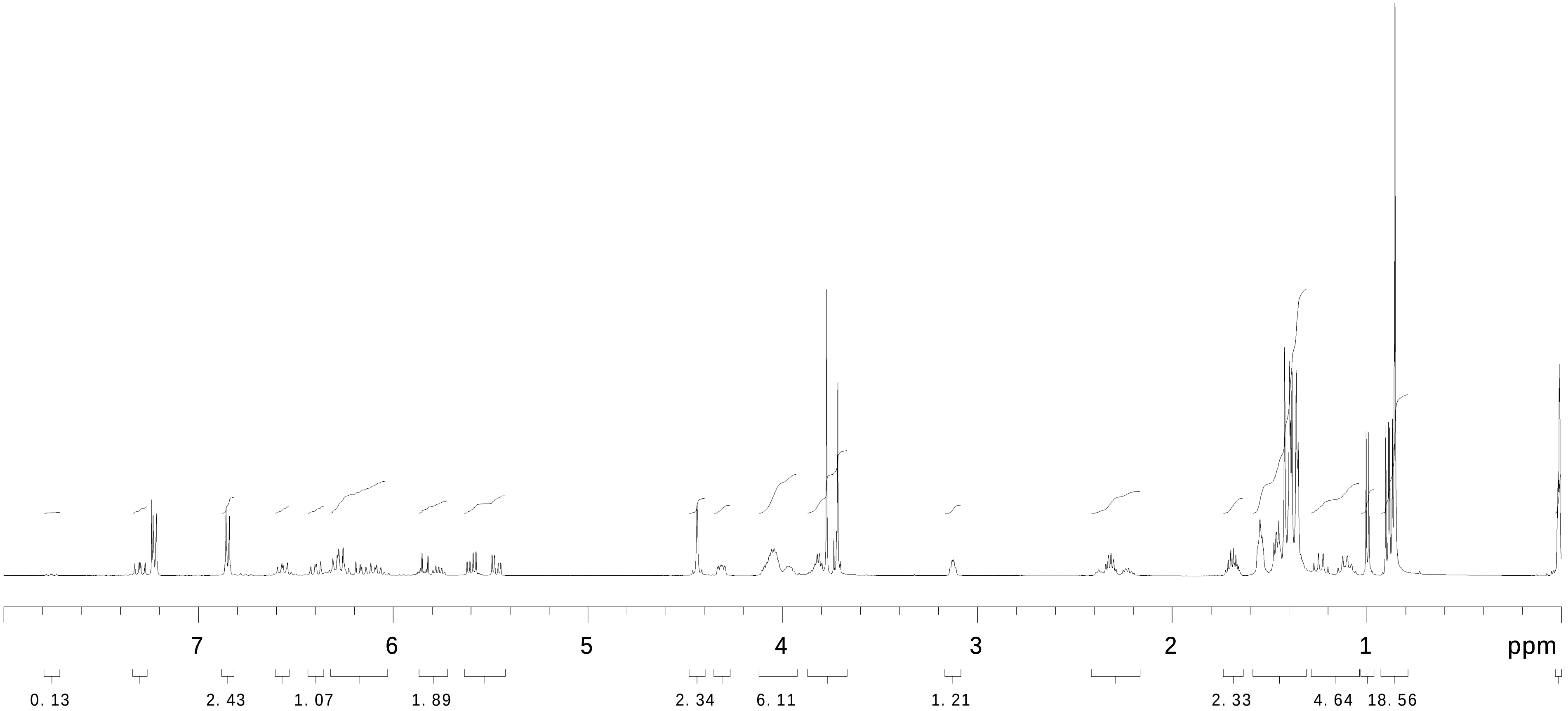
OBSERVE C13, 100.6189875
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 21 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-075-2-carbon



25



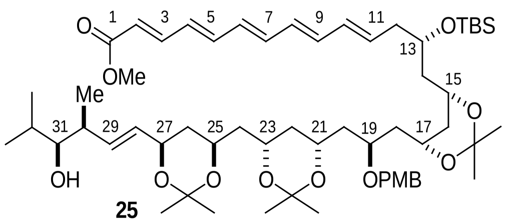
Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
65 repetitions

OBSERVE H1, 500.3674485

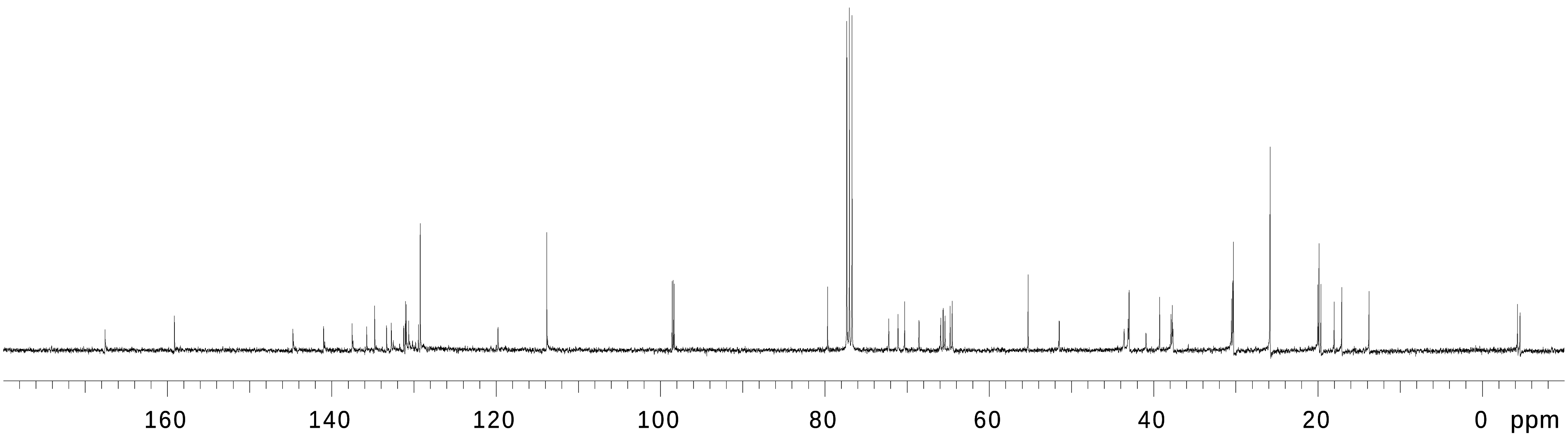
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-076-n1-proto

University of Colorado at Boulder NMR



25



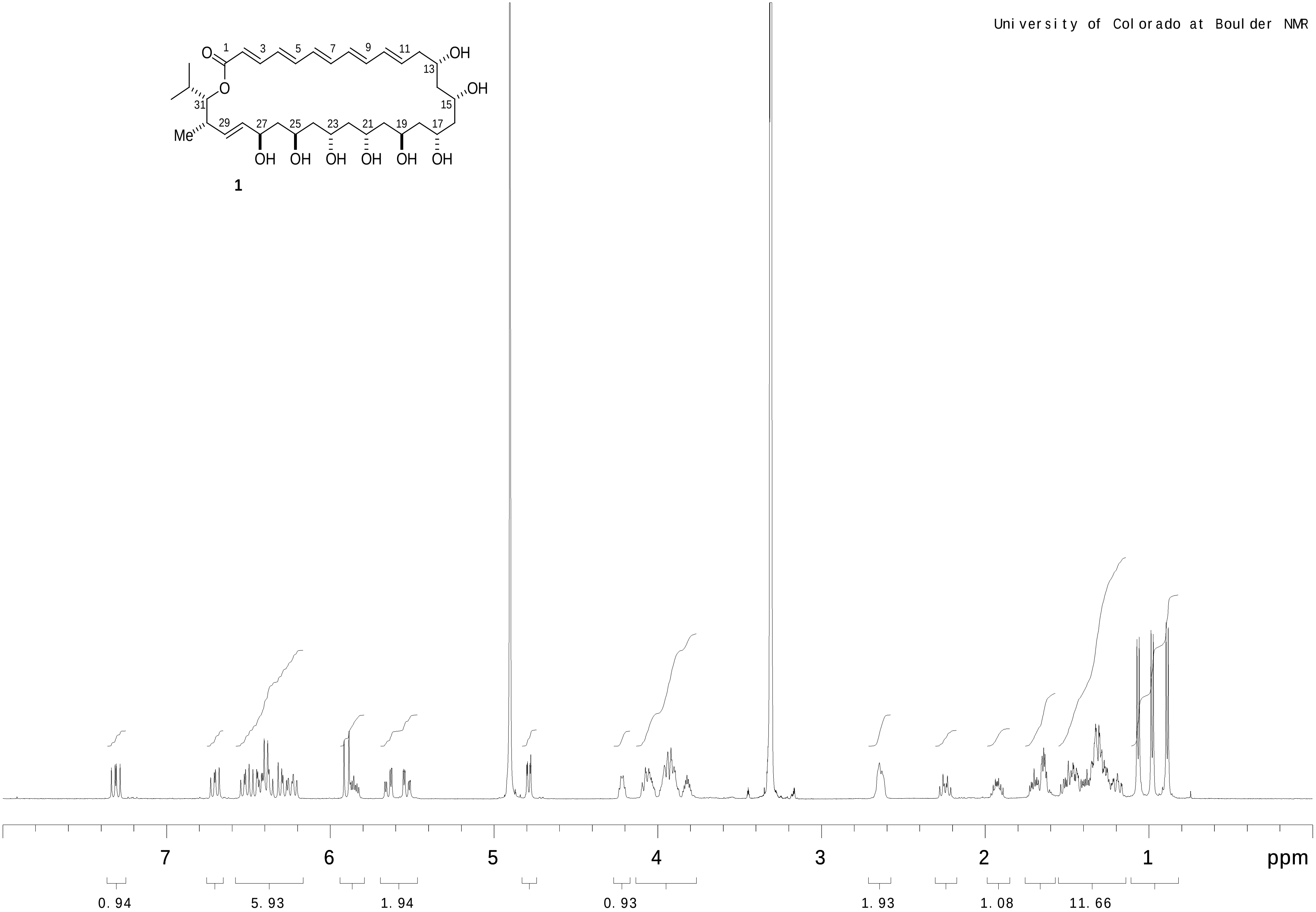
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.309 sec
Width 25039.1 Hz
1024 repetitions

OBSERVE C13, 100.6189890
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 47 minutes

Solvent: CDCl3
Ambient temperature
File: ajc9-076-1-carbon

University of Colorado at Boulder NMR



1

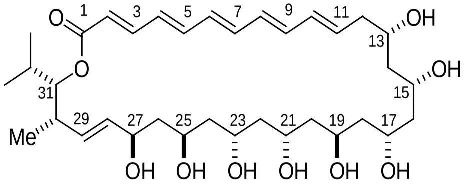
Relax. delay 1.500 sec
Pulse 20.8 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
641 repetitions

OBSERVE H1, 500.3694077

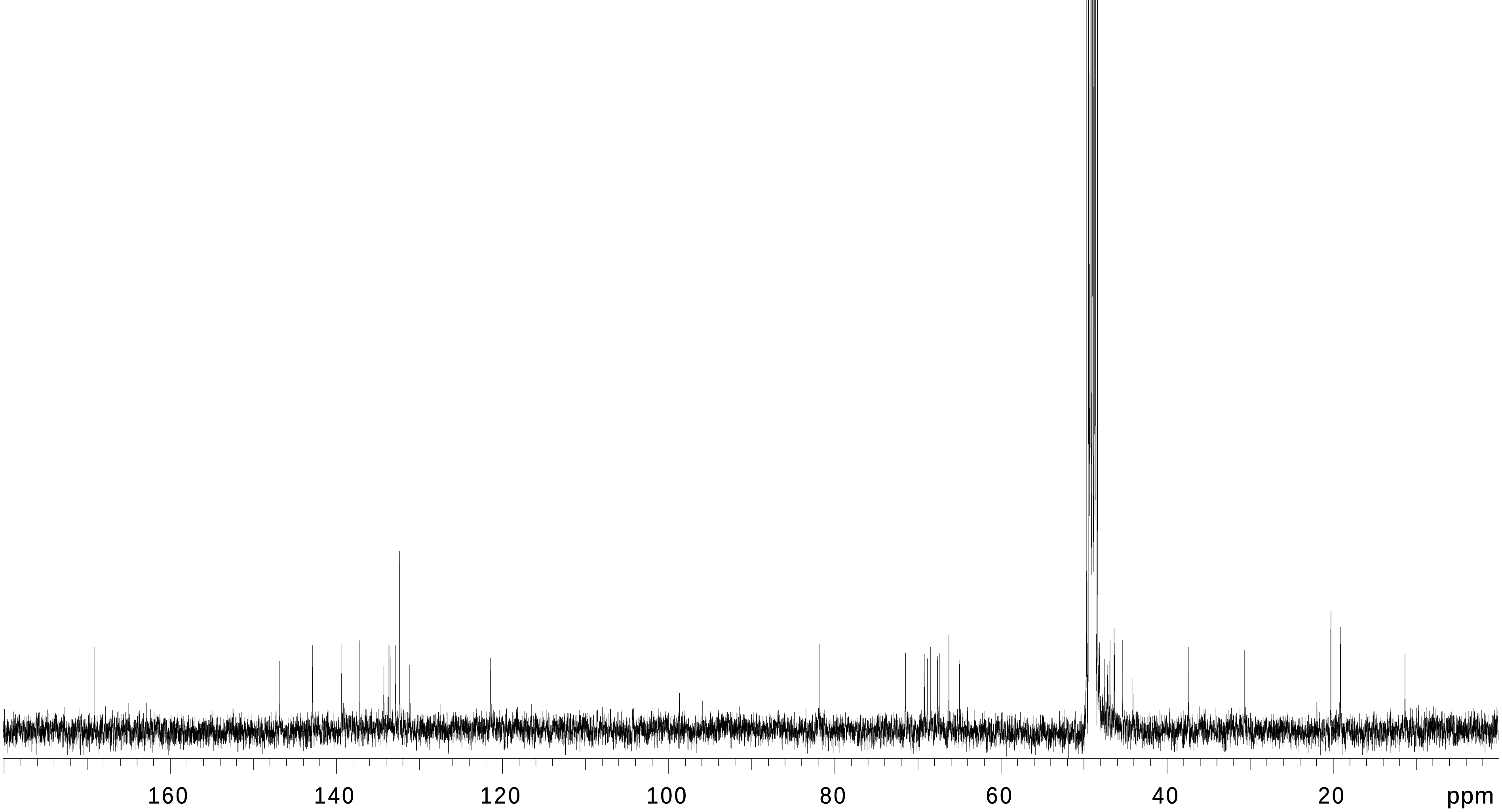
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 48 minutes

Solvent: CD3O
Ambient temperature
File: ajc9-082-RK397proton

University of Colorado at Boulder NMR



1



Relax. delay 1.000 sec
Pulse 60.0 degrees
Acq. time 1.309 sec
Width 25039.1 Hz
20352 repetitions

OBSERVE C13, 100.6192379
DECOUPLE H1, 400.1590573
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 13.1 hours

Solvent: CD3O
Ambient temperature
File: ajc9-082-RK397carbon